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Agency

Office of Water
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EPA

DRAFT WATER QUALITY CRITERIA METHODOLOGY: HUMAN HEALTH

FEDERAL REGISTER NOTICE

ENVIRONMENTAL PROTECTION AGENCY

[WH-FRL-]

Draft Water Quality Criteria Methodology Revisions: Human Health

AGENCY: U.S. Environmental Protection Agency (EPA).

ACTION: Notice of Draft Revisions to the Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health

SUMMARY: EPA is announcing the availability for public comment of draft revisions to the Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health ("AWQC Methodology Revisions") published pursuant to Section 304(a)(1) of the Clean Water Act (CWA). These AWQC Methodology Revisions, once finalized, will supersede the existing **Guidelines and Methodology Used in the Preparation of Health Effect Assessment Chapters of the Consent Decree Water Criteria Documents ("1980 AWQC National Guidelines"),** published by EPA in November 1980 (45 FR 79347, Appendix C). Today's Notice is intended to satisfy the requirements of Section 304(a)(1) of the CWA that EPA periodically revise criteria for water quality to accurately reflect the latest scientific knowledge on the kind and extent of all identifiable effects on health and welfare that may be expected from the presence of pollutants in any body of water, including ground water. These AWQC Methodology Revisions are necessitated by the many significant scientific advances that have occurred during the past 17 years in such key areas as cancer and noncancer risk assessments, exposure assessments, and bioaccumulation. These revisions are not regulations and do not

impose legally-binding requirements on EPA, States, Territories, Tribes, or the public. Also published as part of this Notice are draft AWQC criteria document summaries for three contaminants that reflect the Draft AWQC Methodology Revisions.

AVAILABILITY OF DOCUMENTS: The Draft AWQC Methodology Revisions are published below. Copies of the technical support document and the three complete criteria documents cited in this Notice may be obtained from the U.S. EPA National Center for Environmental Publications and Information (NCEPI), 11029 Kenwood Road, Cincinnati, OH 45242 or (513) 489-8190. Materials in the public docket will be available for public inspection and copying during normal business hours at the Office of Water Docket, 401 M St., S.W., Washington, D.C. 20460 by appointment only. Appointments may be made by calling (202) 260-3027 and requesting item W-97-20. A reasonable fee will be charged for photocopies.

Selected documents supporting the Draft AWQC Methodology Revisions will also be available for viewing by the public at the following locations:

I. Region 1 Library, JFK Federal Building, One Congress Street, Boston, MA 02203 (617) 565-3300

II. Region 2 Library, 290 Broadway, 16th Floor, New York, NY 10007 (212) 637-3185

III. Region 3 Library, 841 Chestnut Building, Philadelphia, PA 19107 (215) 566-5254

IV. Region 4 Library, Atlanta Federal Center, 61 Forsyth St, SW, 9th Floor Tower, Atlanta, GA 30303-3104 (404) 347-4216

V. Region 5 Library, 77 West Jackson Boulevard, Chicago, IL 60604-3590 (312) 353-2022

VI. Region 6 Library, 1445 Ross Avenue, Dallas, TX 75202 (214) 665-6424

VII. Region 7 Information Resource Center, 726 Minnesota Avenue, Kansas City, KS 66101-2728 (913) 551-7241

VIII. Region 8 Library, 999 18th Street, Suite 500, Denver, CO 80202-2466 (303) 312-6746

IX. Region 9 Library, 75 Hawthorne Street, San Francisco, CA 94105 (415) 744-1517

X. Region 10 Library, 1200 Sixth Avenue, Seattle, WA 98101 (206) 553-1289

DATES: EPA will accept public comments on the Draft AWQC Methodology Revisions until 120 days from the publication date. Comments postmarked after this date may not be considered.

ADDRESSEES: An original and three copies of all comments and enclosures, including references, on the draft AWQC Methodology Revisions should be addressed to the W-97-20 Docket Clerk, Water Docket (4101), U.S. EPA, 401 M St., S.W., Washington, D.C. 20460. Electronic comments must be submitted as a WordPerfect 5.1 or WP6.1 file or as an ASCII file avoiding the use of special characters. Comments and data will also be accepted on disks in WordPerfect 5.1 or WP 6.1or ASCII file format. Electronic comments on this Notice may be filed via e-mail at: ow-docket@epamail.epa.gov. Commenters who want EPA to acknowledge receipt of their comments should include a self-addressed stamped envelope. No facsimiles (faxes) will be accepted.

FOR FURTHER INFORMATION CONTACT: Denis Borum (4304), U.S. EPA, 401 M St. S.W., Washington, D.C. 20460 (Telephone: (202) 260-8996).

SUPPLEMENTARY INFORMATION:

List of Acronyms Used

ADI	Acceptable Daily Intake
ARAR	Applicable or Relevant and Appropriate Requirements
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
CTR	California Toxics Rule
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
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 BIPHENYLS
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 Retrieval
TCDD-dioxin	Tetrachlorodibenzo-*p*-dioxin
TEAM	Total Exposure Assessment Methodology
TEF	Toxicity Equivalency Factor
TMDL	Total Maximum Daily Load

TSD	Technical Support Document
USDA	United States Department of Agriculture
UF	Uncertainty Factor
WQBEL	Water Quality-Based Effluent Limits

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Summary of Today's Action

Background

Section 304 (a)(1) of the Clean Water Act requires EPA to develop and periodically revise criteria for water quality accurately reflecting the latest scientific knowledge. In 1980, EPA published ambient water quality criteria (AWQC) for 64 pollutants/pollutant classes and provided a methodology for deriving the criteria. The 1980 AWQC National Guidelines for developing human health AWQC addressed three types of endpoints: noncancer, cancer and organoleptic (taste and odor) effects. Criteria values for the protection against noncancer and cancer effects were estimated by using risk assessment-based procedures, including extrapolation from animal toxicity or human epidemiological studies. Basic human exposure assumptions were applied to the criterion equation, such as: the exposed individual is a 70-kilogram adult male; the assumed consumption of freshwater and estuarine fish and shellfish is 6.5 grams/day; and the assumed ingestion rate of drinking water is 2 liters/day. When using cancer as the critical risk assessment endpoint, which was assumed not to have a threshold, the AWQC were presented for information purposes as a range of concentrations associated with specified incremental lifetime risk levels (i.e., a range from 10^{-5} to 10^{-7}). When using noncancer effects as the critical endpoint, the AWQC reflected an assessment of a "no-effect" level, since noncancer effects generally exhibit a threshold.

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 to quantify cancer risks at low doses to replace the current default use of the linearized multistage (LMS) model. In noncancer risk assessment, the Agency is moving toward the use of the benchmark dose (BMD) and other dose-response approaches in place of the traditional NOAEL approach to estimate a reference dose or concentration. 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 that EPA has reflected in the Draft AWQC Methodology Revisions. In addition, more formalized procedures are now available to account for human exposure to multiple sources when setting health goals such as AWQC that have addressed only one exposure source. With respect to bioaccumulation, the Agency has moved toward the use of a bioacumulation factor (BAF) to reflect the uptake of a contaminant from all sources (e.g., ingestion, sediment) by fish and shellfish, rather than just from the water column as reflected by the use of a bioconcentration factor (BCF) as included in the 1980 methodology. The Agency has developed detailed procedures and guidelines for estimating BAF values.

EPA Human Health Risk Assessment Guidelines Developed 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). The Agency also issued guidelines for assessing the health risks to chemical mixtures in 1986 (51 FR 34014). 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). The guidelines for assessing reproductive toxicity were subsequently updated and finalized (61 FR 56274) in 1996. In 1991, the Agency also developed an external review draft of revised risk assessment guidelines for noncancer health effects. In 1995, EPA also proposed guidelines for neurotoxicity risk assessment (60 FR 52032).

In addition to these risk assessment guidelines, EPA also published the "Exposure Factors Handbook" in 1989, which presents commonly used Agency exposure assumptions and the surveys from which they are derived. The Exposure Factors Handbook (EPA/600/P-95/002Fa) was updated in 1997. In 1992, EPA published the revised Guidelines for Exposure Assessment (57 FR 22888), which describe general concepts of exposure assessment, including definitions and associated units, and provide guidance on planning and conducting an exposure

assessment. Also, in the 1980s the Agency published the Total Exposure Assessment Methodology (TEAM), which presents a process for conducting comprehensive evaluation of human exposures. 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. In 1997, EPA developed draft Guiding Principles for Monte Carlo analysis.

Also, in 1986, the Agency made available to the public the Integrated Risk Information System (IRIS). IRIS is a data base that contains risk information on the cancer and noncancer effects of chemicals. The IRIS assessments are peer reviewed and represent EPA consensus positions across the Agency's program offices and regional offices. In 1995, the Agency initiated an IRIS pilot program to test improvements to the internal peer review and consensus processes, and to provide more integrated characterizations of cancer and noncancer health effects.

Differing Risk Assessment and Risk Management Approaches for AWQC and MCLGs

Another reason for these revisions is the need to bridge the gap between the differences 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 CWA and MCLGs (Maximum Contaminant Level Goals) under the Safe Drinking Water Act (SDWA). Three notable differences are with respect to the treatment of chemicals designated as Group C possible human carcinogens under

the 1986 Guidelines for Carcinogen Risk Assessment, the consideration of nonwater sources of exposure when setting an AWQC or MCLG for a noncarcinogen, and cancer risk ranges.

1. *Group C Chemicals*. Chemicals have been typically classified as Group C—i.e., possible human carcinogens—under the existing (1986) EPA cancer classification scheme for any of the following reasons:

1) 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."

2) Tumor response is of marginal significance due to inadequate design or reporting.

3) Benign, but not malignant, tumors occur with an agent showing no response in a variety of short-term tests for mutagenicity.

4) There are responses of marginal statistical significance in a tissue known to have a high or variable background rate.

The 1986 Guidelines for Carcinogen Risk Assessment specifically recognized the need for flexibility with respect to quantifying the risk of Group C agents. The guidelines noted that agents judged to be in Group C, possible human carcinogens, 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 agents with respect to the weight-of-evidence for characterizing them as likely to be carcinogenic to humans. For all pollutants judged as having adequate data for quantifying carcinogenic risk—including those now classified as Group C—AWQC were derived based on data on cancer incidence. 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 agents, the MCLG is usually obtained using an RfD based on its noncancer effects with the application of an additional uncertainty factor of 1 to 10 to account for its possible carcinogenicity. If valid noncancer data for a Group C agent 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 one hundred thousand 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 agent, the drinking water concentrations associated with excess cancer risks in the range of 10^{-5} to 10^{-6} were 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 uncertainty factor to account for potential carcinogenicity when using the RfD approach.

2. *Consideration of Nonwater Sources of Exposure.* The 1980 AWQC National Guidelines for setting AWQC recommended that contributions from nonwater sources, namely air and non-fish dietary intake, 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 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 reflected by the MCLG value. 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 public health 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.

3. *Cancer Risk Ranges.* In addition to the different risk assessment approaches discussed above for deriving AWQC and MCLGs for Group C agents, different risk management approaches have arisen between the drinking water and ambient surface water programs with respect to using lifetime excess risk values when setting health-based criteria for carcinogens. As indicated previously, the surface water program historically derived AWQC for carcinogens that generally corresponded to lifetime excess cancer risk levels of 10^{-7} to 10^{-5}. The drinking water program has set MCLGs for Group C agents based on a slightly less stringent risk range of 10^{-6} to 10^{-5}, while MCLGs for chemicals with strong evidence of carcinogenicity (that is, classified as Group A (known) or B (probable) human carcinogen) 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.

Steps Taken toward Evaluating and Revising the 1980 AWQC National Guidelines

In order to begin developing a "state-of-the-science" approach to revising the 1980 AWQC National Guidelines, EPA prepared an issues paper that described the 1980 methodology, discussed areas that needed strengthening, and proposed revisions. This paper was then distributed for review and comment to experts at EPA headquarters, regional offices, and laboratories; other Federal Agencies, such as the Food and Drug Administration (FDA), the National Institute of Environmental Health Sciences (NIEHS), and the Centers for Disease Control and Prevention (CDC); State health organizations; Canadian health agencies; academe; and environmental, industry, and consulting organizations.

1. September 1992 National Workshop

On September 13-16, 1992, more than 100 invited participants discussed the critical issues in a workshop convened in Bethesda, Maryland. Based on their expertise, attendees were assigned to specific technical work groups. The work group topics were cancer risk, noncancer risk, exposure, microbiology, minimum data, and bioaccumulation. Each work group member received a set of detailed questions that served to focus discussions on critical factors in the 1980

AWQC National Guidelines. After the work group members deliberated separately on their specific technical areas, all workshop participants were given the opportunity to comment on the proceedings. After the workshop concluded, the chairperson for each technical work group prepared a written summary of that group's deliberations and recommendations. Each work group participant was given the opportunity to review and comment on the summaries; these comments were used to prepare a draft of the proposed revision to the methodology.

2. Science Advisory Board Review

After review of the draft of the proposed revisions to the methodology by EPA, the workshop participants, and other relevant parties, a summary document was submitted for review and comment to the Science Advisory Board (SAB) in January 1993 and presented to the Drinking Water Committee of the SAB during its meeting on February 8-9, 1993. The SAB presented its official comments to EPA on August 12, 1993. The SAB comments have been highlighted and addressed in each of the technical areas discussed in Appendix III of this Notice. A complete copy of the document submitted to the SAB and SAB's comments are available in the docket accompanying this Notice.

3. FSTRAC Review

At the Federal State Toxicology and Risk Analysis Committee (FSTRAC) meeting on December 1-3, 1993, in Washington, D.C., several State representatives presented their opinions on the preliminary draft recommendations for revisions to the 1980 AWQC National Guidelines.

A summary of this meeting is presented in a document entitled "Workshop Summary: State Comments on the Preliminary Draft Revisions of the Methodology for Deriving National Ambient Water Quality Criteria for the Protection of Human Health." This document is also available for review in the docket supporting this proposal.

4. Water Quality Guidance for the Great Lakes System

In March 1995, EPA published the Final Water Quality Guidance for the Great Lakes System (60 FR 15366). The Great Lakes Water Quality Guidance, developed under Section 118(c)(2) of the CWA, provides water quality criteria for 29 pollutants as well as methodologies, policies, and procedures for Great Lakes States and Tribes to establish consistent, long-term protection for fish and shellfish in the Great Lakes and their tributaries, as well as for the people and wildlife who consume them. In developing the methodology to derive human health criteria for the waters of the Great Lakes System, the Agency was mindful of the need for consistency with the planned changes in the methodology for deriving national AWQC for the protection of human health presented in today's proposal. Throughout the following text, references are made to comparisons of the two methodologies, national and Great Lakes Water Quality Guidance, especially whenever differences occur due to regional exposure assumptions made for the Great Lakes System.

Major Changes in the Draft AWQC Methodology Revisions

The proposal presents several changes from the 1980 AWQC National Guidelines:

1. EPA's future role in developing AWQC for the protection of human health will include the refinement of the revised methodology, the development of revised criteria for chemicals of high priority and national importance (including, but not limited to chemicals that bioaccumulate, such as PCBs, dioxin, and mercury), and the development or revision of AWQC for some additional priority chemicals. EPA does not plan to completely revise all of the criteria developed in 1980 or those updated as part of the proposed California Toxics Rule (CTR) 62 FR 42160, August 5, 1997. (This rule proposes for California, numeric water quality criteria for priority toxic pollutants necessary to fulfill the requirements of Section 303(c)(2)(b) of the CWA.) Further, EPA intends to revise 304(a) criteria on the basis of one or more components (e.g., BAF, fish intake, toxicological assessment) rather than a full set of components. Appendix II of the FR Notice discusses how the Agency is proposing to implement the methodology and revise the 304(a) criteria. EPA also discusses the role of 304(a) criteria in State/Tribal adoption of water quality standards under Section 303(c) of the CWA, EPA's responsibilities in reviewing and approving State/Tribal standards, and EPA's duties in regards to promulgating State/Tribal standards when necessary.

2. EPA encourages States and Tribes to use the revised methodology, once finalized, to develop or revise AWQC to appropriately reflect local conditions. EPA believes that AWQC inherently require several risk management decisions that are, in many cases, better made at the State and Tribal level (e.g., fish consumption rates, target risk levels). EPA will continue to develop and update necessary toxicological and exposure data needed in the derivation of AWQC that may not be practical for the States or Tribes to obtain. EPA encourages States and Tribes to use local or regional fish consumption data when available.

3. The 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 similarly, by 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 of the general population, is clearly a risk management decision. In many cases, the Agency has selected parameters using its best judgment regarding the overall protection afforded by the resulting AWQC when all parameters are combined. Appendix I discusses in detail the differences between science, science policy, and risk management. Appendix I 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.

4. The Draft AWQC Methodology Revisions provide an alternative to expressing AWQC as a water concentration. AWQC may also be expressed in terms of a fish tissue concentration. For some substances, particularly those that are expected to exhibit substantial bioaccumulation, the AWQC derived using the above equations may have extremely low values, possibly below the practical limits for detecting and quantifying the substance in the water column. It may, therefore, be more practical and meaningful in these cases to focus on the

concentration of those substances in fish tissue, since fish ingestion would be the predominant source of exposure for substances that bioaccumulate.

5. EPA is proposing an incidental water ingestion exposure rate of 0.01 L/day to account for long-term incidental recreational ingestion (i.e., swimming, boating, fishing) for use in those cases where AWQC are developed for recreational waters that are not used as drinking water sources.

6. AWQC for the protection of human health are designed to minimize the risk of adverse effects occurring to humans from chronic (lifetime) exposure to substances through the ingestion of drinking water and consumption of fish obtained from surface waters. The Agency is not recommending the development of additional water quality criteria similar to the "drinking water health advisories" that focus on acute or short-term effects, since these are not seen routinely as having a meaningful role in the water quality criteria and standards program.

However, there may be some instances where the consideration of short-term toxicity and exposure in the derivation of AWQC is warranted. Although the AWQC are based on chronic health effects data (both cancer and noncancer effects), the criteria are intended to also be protective with respect to adverse effects that may reasonably be expected to occur as a result of elevated short-term exposures. That is, through the use of conservative assumptions with respect to both toxicity and exposure parameters, the resulting AWQC values should provide adequate protection not only for the general population over a lifetime of exposure, but also for special subpopulations who, because of high water- or fish-intake rates, or because of biological

sensitivities, have an increased risk of receiving a dose that would elicit adverse effects from short-term exposures. The Agency recognizes, however, that there may be some cases where the AWQC values based on chronic toxicity may not provide adequate protection for a subpopulation at special risk from such exposures. The Agency encourages States, Tribes, and others employing the proposed methodology to give consideration to such circumstances in deriving criteria to ensure that adequate protection is afforded to all identifiable subpopulations. (Appendix III discusses this in greater detail.)

7. For noncarcinogens, risk managers may select another value within an RfD range rather than the default point estimate RfD value, in criteria development, where a rationale for the range and the value selected can be provided. General guidance for the use of values within the RfD range is provided based on the overall uncertainty associated with the RfD and when adverse health effects in children are not the basis for the RfD. For example, if the IRIS RfD is 1 mg/kg/day and the uncertainty factor (UF) is 1,000, a log-symmetrical order of magnitude around 1 mg/kg/day could be used resulting in a range of 0.3 to 3 mg/kg/day. If the UF were less than 1,000, the overall range would be reduced accordingly (e.g., ½ log for UFs between 100 and 1,000; and no range for UFs of 100 or less). However, EPA would select the point estimate as a default (the midpoint within the range) when calculating a 304(a) criteria value for the purposes of promulgating State or Tribal water quality standards.

8. The Draft AWQC Methodology Revisions reflect EPA's 1996 Proposed Guidelines for Carcinogen Risk Assessment. For instance, mode of action (MoA) information is used to determine the most appropriate low-dose extrapolation approach for carcinogenic agents. The

dose-response assessment under the new guidelines is a two-step process. In the first step, the response data are modeled in the range of empirical observation. Modeling in the observed range is done with biologically based or appropriate curve-fitting modeling. In the second step, extrapolation below the range of observation is accomplished by biologically based modeling if there are sufficient data or by a default procedure (linear, nonlinear, or both). A point of departure for extrapolation is estimated from modeling observed data. The lower 95 percent confidence limit on a dose associated with 10 percent extra risk (i.e., LED_{10}) is proposed as a standard point of departure for low-dose extrapolation. If it is determined that the MoA understanding supports a nonlinear extrapolation, the AWQC is derived using the nonlinear default which is based on a margin of exposure (MoE) analysis for the point of departure (e.g., the LED_{10}) and applying a safety factor(s) in the risk management. The linear default would be considered for those agents that are better supported by the assumption of linearity (e.g., direct DNA reactive mutagens) for their MoA. A linear approach would also be applied when inadequate or no information is available to explain the carcinogenic MoA as a science policy choice in the interest of public health. The linear default is a straight line extrapolation to the origin (i.e., zero dose, zero extra risk) from the point of departure (e.g., LED_{10}) identified in the observable response range. There may be situations where it is appropriate to apply both the linear and nonlinear default procedures (e.g., for an agent that is both DNA reactive and active as a promoter at higher doses).

9. For substances that are carcinogenic, particularly those for which the mode of action suggests nonlinearity at low doses, the Agency recommends that an integrated approach be taken in looking at cancer and noncancer effects, and if one pathway does not predominate, AWQC

values should be determined for both carcinogenic and noncarcinogenic effects. The lower of the resulting values should be used for the AWQC.

10. When deriving AWQC for noncarcinogens and nonlinear carcinogens, a factor must be included to account for other nonwater exposure sources so that the entire RfD, or [Point of Departure (Pdp) divided by a safety factor (SF); (Pdp)/SF)] is not allocated to drinking water and fish consumption alone. Guidance is provided in the revised methodology for determining the factor, referred to as the relative source contribution (RSC), to be used for a particular chemical. The Agency is proposing the use of a decision tree procedure to support the determination of the appropriate RSC value for a given water contaminant. In the absence of data, the Agency will use 20 percent of the RfD as the default RSC in calculating a 304(a) criteria value for the purposes of promulgating State or Tribal water quality standards.

11. When deriving AWQC for linear carcinogens, the Agency recommends that risk levels in the range of 10^{-5} to 10^{-6} be used for the protection of the general population. States and Tribes can always choose a more stringent risk level, such as 10^{-7}. Care should be taken, however, in situations where the AWQC includes fish intake levels based on the general population to ensure that the risk to more highly exposed subgroups (sportfishers or subsistence fishers) does not exceed the 10^{-4} level.

12. The default fish consumption values are 17.80 grams/day for the general population, which represents the 90th percentile consumption rate for the entire population

(and approximates the average consumption rate for sport anglers, nationally) and 86.30 grams/day for subsistence fishers/minority anglers, which represents the 99th percentile consumption rate for the general population and is within the range of average intakes for subsistence fishers/minority anglers (comments are requested on alternatively using 39.04 grams/day for subsistence fishers/minority anglers, which is lower in the range of averages). These values are derived from the United States Department of Agriculture's (USDA) Continuing Survey of Food Intake by Individuals (CSFII) from 1989-1991. These rates replace the single default value of 6.5 grams/day used in the 1980 AWQC National Guidelines. These default values are chosen to be protective of the majority of the individuals in those groups. However, States and Tribes are urged to use a fish intake level derived from local data on fish consumption in place of these default values when deriving AWQC, ensuring that the fish intake level chosen be protective of highly exposed individuals in the population. Consumption rates for women of childbearing age and children younger than 14 are also provided to maximize protection in those cases where these subpopulations may be at greatest risk.

13. All criteria should be derived using a BAF rather than a BCF, which was used in the 1980 AWQC National Guidelines. The BAF should be developed using the EPA methodology or any method consistent with the EPA method. EPA's highest preference in developing BAFs are BAFs based on field-measured data from local/regional fish.

14. EPA is neither setting organoleptic criteria nor a default methodology for deriving such criteria. Such criteria will necessitate case-by-case analysis.

The attached document includes six major sections: Appendix I, which discusses the purpose of the methodology, the background associated with the original methodology and the need for revision, and the major changes in the revised methodology; Appendix II, which addresses implementation issues associated with the methodology; Appendix III, which presents the main scientific areas that make up the methodology (cancer, noncancer, exposure, and bioaccumulation methods); and Appendices IV through VI, which present summaries of the three criteria developed for inclusion with the revised methodology. Complete versions of the three criteria documents are available on the Internet at http://www.epa.gov/OST/Rules/index.html#open.

This notice proposes revisions to EPA's 1980 methodology for the development of water quality criteria to protect human health. The revisions reflect scientific advancements since 1980 in a number of areas, including cancer and noncancer risk assessments, exposure assessments and bioaccumulation. When final, the revised methodology will provide guidance to States, Tribes, and the public on the approach that EPA expects to take in developing recommended human health criteria. The revised methodology also will provide guidance to States and Tribes that they may use in developing human health criteria as part of their water quality standards; States and Tribes use such standards in implementing a number of environmental programs, including setting discharge limits in NPDES permits. The revised methodology does not substitute for the

Clean Water Act or EPA's regulations; nor is it a regulation itself. Thus, the revised methodology cannot impose legally-binding requirements on EPA, States, or the public, and may not apply to a particular situation based upon the circumstances. EPA and State decisionmakers retain the discretion to use different, scientifically defensible, methodologies to develop human health criteria. EPA may change the methodology in the future.

This criteria methodology incorporates scientific advancements made over the past two decades. The use of this methodology is an important component of the Agency's efforts to improve the quality of the Nation's waters. EPA believes the methodology will enhance the overall scientific basis of water quality criteria. Further, the methodology should help States and Tribes address their unique water quality issues and risk management decisions, and afford them greater flexibility in developing their water quality programs.

Dated:

J. Charles Fox
Acting Assistant Administrator for Water

Appendix I. Background

A. Water Quality Criteria and Standards

1. Water Quality Criteria and the Criteria Derivation Methodology

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) 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 may be used as guidance by States and Tribes to establish water quality standards, which 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.

This revised methodology addresses 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. When finalized, the Agency intends to use the revised AWQC human health methodology to both develop new AWQC for additional chemicals and to revise

existing AWQC. Appendices IV-VI are summaries of criteria developed using the revised methodology. These AWQC were developed to demonstrate the different risk assessment and exposure approaches presented in the revised methodology. The complete criteria documents are available from NTIS or on EPA's Internet web site. 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. 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 revised methodology also defines the default factors EPA intends to use in evaluating and determining consistency of State water quality standards with the requirements of the CWA. The Agency intends to use these default factors to calculate water quality criteria when promulgating water quality standards for a State or Tribe under Section 303(c) of the Act.

2. Summary of the 1980 AWQC National Guidelines

The 1980 AWQC National Guidelines for developing AWQC for the protection of human health addressed three types of endpoints: noncancer, cancer, and organoleptic (taste and odor) effects. Criteria values for protection against noncancer and cancer effects were estimated by using risk assessment-based procedures, including extrapolation from animal toxicity or human

epidemiological studies. Basic human exposure assumptions were applied, such as: the exposed individual is a 70-kilogram adult male; the assumed consumption of freshwater and estuarine fish and shellfish is 6.5 grams per day; and the assumed ingestion rate of drinking water is 2 liters per day.

When using cancer as the critical risk assessment endpoint, which has been assumed not to have a threshold, the AWQC were presented as a range of concentrations associated with specified incremental lifetime risk levels[1] (i.e., a range from 10^{-5} to 10^{-7}). When using noncancer effects as the endpoint, the AWQC reflected an assessment of a "no-effect" level, since noncancer effects generally exhibit a threshold. The risk assessment-based procedures used to derive the AWQC to protect human health were specific to whether the endpoint was cancer or noncancer. The key features of each procedure are described briefly in the following sections.

Cancer effects. If human or animal studies on a contaminant indicated that it induced a statistically significant carcinogenic response, the 1980 AWQC National Guidelines treated the contaminant as a carcinogen and derived a low-dose cancer potency factor from available animal data using the linearized multistage model (LMS). The LMS, which uses a linear, nonthreshold assumption for low-dose risk, was used by the Agency as a science policy choice in protecting public health, and represents the most plausible upper limit for low-dose risk. The cancer potency factor, which expresses incremental, lifetime risk as a function of the rate of intake of the contaminant, was then combined with exposure assumptions to express that risk in terms of an ambient water

[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.

concentration. In the 1980 AWQC National Guidelines, the Agency presented a range of contaminant concentrations corresponding to incremental cancer risks of 10^{-7} to 10^{-5} (that is, a risk of one additional case of cancer in a population of ten million to one additional cancer case in a population of one hundred thousand, respectively). The risk range was presented for information purposes and did not represent an Agency judgment on "acceptable" risk level. The Agency stated in 1980 that: "for the maximum protection of human health from the potential carcinogenic effects due to exposure of Chemical X through ingestion of contaminated water and aquatic organisms, the ambient water concentration should be zero based on the nonthreshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental cancer risk over the lifetime are estimated at 10^{-5}, 10^{-6}, and 10^{-7}."

Noncancer effects. If the pollutant was not considered to have the potential for causing cancer in humans (this was later defined as a known, probable, or possible human carcinogen by the 1986 Guidelines for Cancer Risk), the 1980 AWQC National Guidelines treated the contaminant as a noncarcinogen, and a criterion was derived using a threshold concentration for noncancer adverse effects. The criteria derived from noncancer data were based on the Acceptable Daily Intake (ADI) (now termed the reference dose [RfD]). ADI values were generally derived using no-observed-adverse-effect level (NOAEL) data from animal studies, although human data were used whenever available. The ADI was calculated by dividing the NOAEL by an uncertainty factor to account for uncertainties inherent in extrapolating toxicological data from animal studies to humans. In accordance with the National Research Council recommendations of 1977, safety factors (later termed uncertainty factors) of 10, 100, or 1,000 were used, depending on the quality and quantity of the data.

Organoleptic effects. Organoleptic characteristics were also used in developing criteria for some contaminants to control undesirable taste and/or odor imparted by them to ambient water. In some cases, a water quality criterion based on organoleptic effects would be more stringent than a criterion based on toxicologic endpoints. The 1980 AWQC National Guidelines emphasized that criteria derived for organoleptic endpoints are not based on toxicologic information, have no direct relationship to adverse human health effects and, therefore, do not necessarily represent approximations of acceptable risk levels for humans.

3. Water Quality Standards

Under Section 303 of the CWA, States have the primary responsibility to establish water quality standards, defined under the Act as designated beneficial uses of a water segment and the water quality criteria necessary to support those uses. Additionally, Native American Tribes authorized to administer the water quality standards program under 40 CFR 131.8 establish water quality standards for waters within their jurisdictions. This statutory framework allows States and Tribes to work with local communities to establish appropriate designated uses, and adopt criteria to protect those designated uses. Section 303 provides for EPA review of Water Quality Standards and for promulgation of a superseding Federal rule in cases where State or Tribal standards are not consistent with the applicable requirements of the CWA, or in situations where the Agency determines Federal standards are necessary to meet the requirements of the Act. Section 303(c)(2)(B) specifically requires States and Tribes to adopt AWQC for toxics for which EPA has published criteria under Section 304(a), and for which the discharge or presence could reasonably be expected to interfere with the designated use adopted by the State or Tribe. In adopting such

criteria, States and Tribes must establish numerical values based on one of the following: (1) 304(a) criteria; (2) 304(a) criteria modified to reflect site-specific conditions; or, (3) other scientifically defensible methods.

In order to avoid confusion, it must be recognized that the Act uses the term "criteria" in two separate ways. In Section 303(c), the term is part of the definition of a water quality standard. That is, a water quality standard is composed of designated uses and the criteria necessary to protect those uses. Thus, States and Tribes are required to adopt regulations which contain legally enforceable criteria. However, in Section 304(a) the term criteria is used to describe the scientific information that EPA develops to be used as guidance in the State, Tribal, or Federal adoption of water quality standards pursuant to 303(c). Thus, two distinct purposes are served by the 304(a)criteria. The first is as guidance to the States and Tribes in the development and adoption of water quality criteria which will protect designated uses, and the second is as the basis for promulgation of a superseding Federal rule when such action is necessary.

B. Need for Revision of the 1980 AWQC National Guidelines

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 to quantify cancer risk at low doses to replace the current default use of the LMS model. (See discussion in Appendix III, Section A.) In noncancer risk assessment, the Agency is moving toward the use of the benchmark dose (BMD) and other dose-response approaches in place of the traditional NOAEL approach to estimate a reference dose or concentration. A BMD is calculated by fitting a mathematical dose-response model to data using appropriate statistical procedures. (See discussion in Appendix III, Section B.)

In exposure analysis, several new studies have addressed water consumption and fish-tissue consumption. These studies provide a more current and comprehensive description of national, regional, and special-population consumption patterns that EPA has reflected in the Draft AWQC Methodology Revisions presented today. In addition, more formalized procedures are now available to account for human exposure from multiple sources when setting health goals such as AWQC that address only one exposure source. (See discussion in Appendix III, Section C.)

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

2. EPA Human Health Risk Assessment Guidelines Development Since 1980

When the 1980 AWQC methodology was 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 proposed revised guidelines for carcinogenic 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). The Agency also issued guidelines for assessing the health risks to chemical mixtures in 1986 (51 FR 34014). 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). The guidelines for assessing reproductive toxicity were subsequently updated and finalized (61 FR 56274) in 1996. In 1991, the Agency also developed an external review draft of revised risk assessment guidelines for noncancer health effects. In 1995, EPA also proposed guidelines for neurotoxicity risk assessment (60 FR 52032).

In addition to these risk assessment guidelines, EPA also published the "Exposure Factors Handbook" in 1989, which presents commonly used Agency exposure assumptions and the surveys from which they are derived. The Exposure Factors Handbook (EPA/600/P-95/002Fa) was updated in 1997. In 1992 EPA published the revised Guidelines for Exposure Assessment (57 FR 22888), which describe general concepts of exposure assessment, including definitions and associated units, and provide guidance on planning and conducting an exposure assessment. Also, in the 1980s the Agency published the Total Exposure Assessment Methodology (TEAM), which presents a process for conducting comprehensive evaluation of human exposures. 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. In 1997, EPA developed draft Guiding Principles for Monte Carlo analysis.

Also, in 1986, the Agency made available to the public the Integrated Risk Information System (IRIS). IRIS is a data base that contains risk information on the cancer and noncancer effects of chemicals. The IRIS assessments are peer reviewed and represent EPA consensus positions across the Agency's program and regional offices. In 1995, the Agency initiated an IRIS pilot program to test improvements to the internal peer review and consensus processes, and to provide more integrated characterizations of cancer and noncancer health effects.

3. Differing Risk Assessment and Risk Management Approaches for AWQC and MCLGs

There are some differences 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 CWA and MCLGs (Maximum Contaminant Level Goals) under the Safe Drinking Water Act (SDWA). Two notable differences are with respect to the treatment of chemicals designated as Group C possible human carcinogens under the 1986 Guidelines for Carcinogen Risk Assessment and the consideration of nonwater sources of exposure when setting an AWQC or MCLG for a noncarcinogen.

Group C Chemicals. Chemicals have been typically classified as Group C—i.e., possible human carcinogens—under the existing (1986) EPA cancer classification scheme for any of the following reasons:

1. 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."

2. Tumor response is of marginal significance due to inadequate design or reporting.

3. Benign, but not malignant, tumors occur with an agent showing no response in a variety of short-term tests for mutagenicity.

4. There are responses of marginal statistical significance in a tissue known to have a high or variable background rate.

The 1986 Guidelines for Carcinogen Risk Assessment specifically recognized the need for flexibility with respect to quantifying the risk of Group C agents. The guidelines noted that agents judged to be in Group C, possible human carcinogens, 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 agents with respect to the weight-of-evidence for characterizing them as likely to be carcinogenic to humans. For all pollutants judged as having adequate data for quantifying carcinogenic risk—including those now classified as Group C—AWQC were derived based on data on cancer incidence. 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 agents, the MCLG is usually obtained using an RfD based on its noncancer effects with the application of an additional uncertainty factor of 1 to 10 to account for its possible carcinogenicity. If valid noncancer data for a Group C agent 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 one hundred thousand 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 agent, the drinking water concentrations associated with excess cancer risks in the range of 10^{-5} to 10^{-6} were 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 uncertainty factor to account for potential carcinogenicity when using the RfD approach.

Consideration of Nonwater Sources of Exposure. The 1980 AWQC National Guidelines for setting AWQC recommended the use of the following equation to derive the criterion:

$$C = \frac{[ADI - (DT + IN)]}{[2 + 0.0065R]} \qquad \text{(Equation IB-1)}$$

where:

C	=	The criterion value
ADI	=	Acceptable daily intake (mg/kg-day)
DT	=	Non-fish dietary intake (mg/kg-day)
IN	=	Inhalation intake (mg/kg-day)
2	=	Assumed daily water intake (L/day)
0.0065	=	Assumed daily fish consumption (kg)
R	=	Bioconcentration factor (L/kg)

As implied by this equation, the contributions from nonwater 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 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 reflected by the MCLG value. 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 public health 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.

Cancer Risk Ranges. In addition to the different risk assessment approaches discussed above for deriving AWQC and MCLGs for Group C agents, different risk management approaches have arisen between the drinking water and ambient surface water programs with respect to using lifetime excess risk values when setting health-based criteria for carcinogens. As indicated previously, the surface water program has derived 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 agents based on a slightly less stringent risk range of 10^{-6} to 10^{-5}, while MCLGs for chemicals with strong evidence of carcinogenicity (that is, classified as Group A, known, or B probable, human carcinogen) 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.

C. Steps Taken toward Evaluating and Revising the 1980 AWQC National Guidelines

In order to begin developing a "state-of-the-science" approach to revising the 1980 AWQC National Guidelines, EPA prepared an issues paper that described the 1980 methodology, discussed areas that needed strengthening, and proposed revisions. This paper was then distributed for review and comment to experts at EPA headquarters, regional offices, and laboratories; other Federal Agencies, such as the Food and Drug Administration (FDA), the National Institute of Environmental Health Sciences (NIEHS), and the Centers for Disease Control and Prevention (CDC); State health organizations; Canadian health agencies; academe; and environmental, industry, and consulting organizations.

1. September 1992 National Workshop

On September 13-16, 1992, more than 100 invited participants discussed the critical issues in a workshop convened in Bethesda, Maryland. Based on their expertise, attendees were assigned to specific technical work groups. The work group topics were cancer risk, noncancer risk, exposure, microbiology, minimum data, and bioaccumulation. Each work group member received a set of detailed questions that served to focus discussions on critical factors in the 1980 AWQC National Guidelines. After the work group members deliberated separately on their specific technical areas, all workshop participants were given the opportunity to comment on the proceedings. After the workshop concluded, the chairperson for each technical work group prepared a written summary of that group's deliberations and recommendations. Each work group participant was given the opportunity to review and comment on the summaries; these comments were used to prepare an initial draft of the revised methodology.

2. Science Advisory Board Review

After review of the initial draft of the revisions to the methodology by EPA, the workshop participants, and other relevant parties, a summary document was submitted for review and comment to the Science Advisory Board (SAB) in January 1993 and presented to the Drinking Water Committee of the SAB during its meeting on February 8-9, 1993. The SAB presented its official comments to EPA on August 12, 1993. The SAB comments have been highlighted and addressed in each of the technical areas discussed in Appendix III of this Notice. A complete copy of the document submitted to the SAB and SAB's comments are available in the docket supporting this Notice.

3. FSTRAC Review

At the Federal State Toxicology and Risk Analysis Committee (FSTRAC) meeting on December 1-3, 1993, in Washington, D.C., several State representatives presented their opinions on the initial draft revised methodology and the SAB's comments. A summary of this meeting is presented in a document entitled "Summary Report: State Comments on the Proposed Revision of the Methodology for Deriving National Ambient Water Quality Criteria for the Protection of Human Health." This document is also available for review in the docket supporting this Notice.

4. Water Quality Guidance for the Great Lakes System

In March 1995, EPA published the Final Water Quality Guidance for the Great Lakes System (60 FR 15366). The Great Lakes Water Quality Guidance, developed under Section 118(c)(2) of the CWA, provides water quality criteria for 29 pollutants as well as methodologies, policies, and procedures for Great Lakes States and Tribes to establish consistent, long-term protection for fish and shellfish in the Great Lakes and their tributaries, as well as for the people and wildlife who consume them. In developing the methodology to derive human health criteria for the waters of the Great Lakes System, the Agency was mindful of the need for consistency with the planned changes in the methodology for deriving national AWQC for the protection of human health presented today. Throughout the following text, references are made to comparisons of the two methodologies, national and Great Lakes Water Quality Guidance, especially whenever differences occur due to regional exposure assumptions made for the Great Lakes System.

D. Overview of AWQC Methodology Revisions, Major Changes, and Issues

Following is a summary of the major revisions to the 1980 AWQC National Guidelines:

1. EPA's future role in developing AWQC for the protection of human health will include the refinement of the revised methodology, the development of revised criteria for chemicals of high priority and national importance (including, but not limited to chemicals that bioaccumulate, such as PCBs, TCDD-dioxin, and mercury), and the development or revision of AWQC for some additional priority chemicals. EPA does not plan to completely revise all of the criteria developed in 1980 or those updated as part of either the 1992 National Toxics Rule (NTR) or the 1997 proposed California Toxics Rule (CTR). Partial updates of all criteria may be plausible. (Appendix II discusses how the Agency is proposing to implement the methodology and update or revise the 304(a) criteria.)

2. EPA encourages States and Tribes to use the revised methodology, once finalized, to develop or revise AWQC to appropriately reflect local conditions. EPA believes that AWQC inherently require several risk management decisions that are, in many cases, better made at the State, Tribal, and local level (e.g., fish consumption rates, target risk levels). EPA will continue to develop and update necessary toxicological and exposure data needed to use in the derivation of AWQC that may not be practical to obtain at the State, Tribal, or local level. EPA encourages States and Tribes to use local or regional fish consumption data when available.

3. 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 similarly, by 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 regarding 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 Section E. 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 effects are:[2]

[2] The fish intake (FI) and bioaccumulation factor (BAF) parameters are presented here in simplified form. It is preferable to calculate criteria by splitting these out by trophic level since bioaccumulation may vary significantly from one level to another. This is discussed further in the bioaccumulation section and specific guidance is given in the Technical Support Document for this methodology. Also, the proposed example criteria that accompany these proposed revisions use trophic level breakouts for these parameters.

Noncancer Effects[3]

$$AWQC = RfD \cdot RSC \cdot \left(\frac{BW}{DI+(FI \cdot BAF)} \right) \qquad \text{(Equation ID-1)}$$

Nonlinear Cancer Effects

$$AWQC = \frac{Pdp}{SF} \cdot RSC \cdot \left(\frac{BW}{DI+(FI \cdot BAF)} \right) \qquad \text{(Equation ID-2)}$$

Linear Cancer Effects

$$AWQC = RSD \cdot \left(\frac{BW}{DI + (FI \cdot BAF)} \right) \qquad \text{(Equation ID-3)}$$

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}

[3] Although appearing in this equation as a factor to be multiplied, the RSC can also be an amount subtracted. Refer to the explanation key below the equations.

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^{-6})
RSC	=	Relative source contribution factor to account for nonwater 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 = 0.01780 kg/day for general adult population and sport anglers, and 0.08630 kg/day for subsistence fishers)
BAF	=	Bioaccumulation factor, lipid normalized (L/kg)

4. As an alternative to expressing AWQC as a water concentration as provided in the above equations, AWQC may also be expressed in terms of a fish tissue concentration. For some substances, particularly those that are expected to exhibit substantial bioaccumulation, the AWQC derived using the above equations may have extremely low values, possibly below the practical limits for detecting and quantifying the substance in the water column. It may, therefore, be more practical and meaningful in these cases to focus on the concentration of those substances in fish tissue, since fish ingestion would be the predominant source of exposure for substances that bioaccumulate. Fish tissue criteria that correspond to an AWQC expressed as a water concentration

obtained from one of the above equations is computed as (note, the BAF used should be the same one that was used to calculate the AWQC):

$$\text{Fish Tissue Criteria (mg/kg or ppm)} = \text{AWQC (mg/L)} \cdot \text{BAF (L/kg)} \qquad \text{(Equation ID-4)}$$

5. EPA is recommending an incidental water ingestion exposure rate of 0.01 L/day to account for long-term incidental recreational ingestion (i.e., swimming, boating, fishing) for use in those cases where AWQC are developed for recreational waters that are not used as drinking water sources.

6. AWQC for the protection of human health are designed to minimize the risk of adverse effects occurring to humans from chronic (lifetime) exposure to substances through the ingestion of drinking water and consumption of fish obtained from surface waters. The Agency is not recommending the development of additional water quality criteria similar to the "drinking water health advisories" that focus on acute or short-term effects, since these are not seen routinely as having a meaningful role in the water quality criteria and standards program. However, as discussed below, there may be some instances where the consideration of acute or short-term toxicity and exposure in the derivation of AWQC is warranted.

Although the AWQC are based on chronic health effects data (both cancer and noncancer effects), the criteria are intended to also be protective with respect to adverse effects that may reasonably be expected to occur as a result of elevated acute or short-term exposures. That is, through the use of conservative assumptions with respect to both toxicity and exposure parameters,

the resulting AWQC values should provide adequate protection not only for the general population over a lifetime of exposure, but also for special subpopulations who, because of high water- or fish-intake rates, or because of biological sensitivities, have an increased risk of receiving a dose that would elicit adverse effects. The Agency recognizes, however, that there may be some cases where the AWQC values based on chronic toxicity may not provide adequate protection for a subpopulation at special risk from shorter-term exposures. The Agency encourages States, Tribes, and others employing the revised methodology to give consideration to such circumstances in deriving criteria to ensure that adequate protection is afforded to all identifiable subpopulations. (See Appendix III, Section C.3 for additional discussion of these subpopulations.)

7. For noncarcinogens, risk managers may select an RfD range rather than a single RfD value, in criteria development, **where a rationale for the range and the value selected can be provided**. General guidance for the use of values within the RfD range is provided based on the overall uncertainty associated with the RfD. For example, if the IRIS RfD is 1 mg/kg/day and the uncertainty factor (UF) is 1,000, a log-symmetrical order of magnitude (i.e., 10-fold) around 1 mg/kg/day could be used resulting in a range of 0.3 to 3 mg/kg/day. If the UF were less than 1,000, the overall range would be reduced accordingly (i.e., ½ log (3-fold) for UFs between 100 and 1,000, resulting in a range of 0.67 to 1.5 mg/kg/day; and no range for UFs of 100 or less). However, EPA intends to select the point estimate as a default (the midpoint within the range) when calculating a 304(a) criteria value for the purposes of promulgating State or Tribal water quality standards. Furthermore, an RfD range should not be used when children are identified as the exposed population of concern.

8. As explained in EPA's 1996 Proposed Guidelines for Carcinogen Risk Assessment, mode of action (MoA) information is used to determine the most appropriate low-dose extrapolation approach for carcinogenic agents. The dose-response assessment under the new guidelines is a two-step process. In the first step, the response data are modeled in the range of empirical observation. Modeling in the observed range is done with biologically based or appropriate curve-fitting modeling. In the second step, extrapolation below the range of observation is accomplished by biologically based modeling if there are sufficient data or by a default procedure (linear, nonlinear, or both). A point of departure for extrapolation is estimated from modeling observed data. The lower 95 percent confidence limit on a dose associated with 10 percent extra risk (LED_{10}) is proposed as a standard point of departure for low-dose extrapolation. If it is determined that the MoA understanding supports a nonlinear extrapolation, the AWQC is derived using the nonlinear default which is based on a margin of exposure (MoE) analysis for the point of departure (LED_{10}) and applying a margin of safety (MoS) in the risk management. The linear default would be considered for those agents that are better supported by the assumption of linearity (e.g., direct DNA reactive mutagens) for their MoA. A linear approach would also be applied when inadequate or no information is available to explain the carcinogenic MoA as a science policy choice in the interest of public health. The linear default is a straight line extrapolation to the origin (i.e., zero dose, zero extra risk) from the point of departure (LED_{10}) identified in the observable response range. There may be situations where it is appropriate to apply both the linear and nonlinear default procedures (e.g., for an agent that is both DNA reactive and active as a promoter at higher doses).

9. For substances that are carcinogenic, particularly those for which the mode of action suggests nonlinearity at low doses, the Agency recommends that an integrated approach be taken

in looking at cancer and noncancer effects, and if one pathway does not predominate, AWQC values should be determined for both carcinogenic and noncarcinogenic effects. The lower of the resulting values should be used for the AWQC.

10. When deriving AWQC for noncarcinogens and nonlinear carcinogens, a factor must be included to account for other nonwater exposure sources so that the entire RfD, or [Point of Departure (Pdp) divided by a safety factor (SF) (Pdp)/SF)] is not allocated to drinking water and fish consumption alone. Guidance is provided in the revised methodology for determining the factor, referred to as the RSC, to be used for a particular chemical. The Agency is recommending the use of a decision tree procedure to support the determination of the appropriate RSC value for a given water contaminant. In the absence of data, the Agency intends to use 20 percent of the RfD as the default RSC in calculating a 304(a) criteria value for the purposes of promulgating State or Tribal water quality standards.

11. For AWQC derived for linear carcinogens, the Agency recommends that risk levels in the range of 10^{-5} to 10^{-6} be used. (See RSD factor in Equation ID-3, above.) States and Tribes can always choose a more stringent risk level, such as 10^{-7}. Care should be taken, however, in situations where the AWQC includes fish intake levels based on the general population to ensure that the risk to more highly exposed subgroups (sportfishers or subsistence fishers) does not exceed the 10^{-4} level.

12. The default fish consumption values in the revised methodology are 17.80 grams/day for the general adult population, which represents the 90th percentile consumption rate for the entire adult population (and approximates the average consumption rate for sport anglers, nationally); and

86.30 grams/day for subsistence fishers/minority anglers, which represents the 99th percentile consumption rate for the general population and falls within the range of averages for subsistence/minority anglers. Public comments are requested on alternatively using 39.04 grams/day, which represents the 95th percentile (and is also within the range of averages), and which of these two values (i.e., 39.04 or 86.30 grams/day) is more representative of fresh/estuarine fish consumption among subsistence fishers/minority anglers. These values are derived from the United States Department of Agriculture's (USDA) Continuing Survey of Food Intake by Individuals (CSFII) from 1989-1991. These rates replace the single default value of 6.5 grams/day used in the 1980 AWQC National Guidelines. These default values are chosen to be protective of the majority of the individuals in those groups. However, States and Tribes are urged to use a fish intake level derived from local data on fish consumption in place of these default values when deriving AWQC, ensuring that the fish intake level chosen be protective of highly exposed individuals in the population. Consumption rates for women of childbearing age and children younger than 14 are also provided to maximize protection in those cases where these subpopulations may be at greatest risk.

13. In the revised methodology, criteria are derived using a BAF rather than a BCF, which was used in the 1980 AWQC National Guidelines. To derive the BAF, States and Tribes may use EPA's methodology or any method consistent with the EPA method. EPA's highest preference in developing BAFs are BAFs based on field-measured data from local/regional fish.

14. EPA is neither setting organoleptic criteria nor recommending a default methodology for deriving such criteria. Such criteria will necessitate case-by-case analysis.

E. Risk Characterization Considerations

1. Background

On March 21, 1995, the EPA Administrator, Carol Browner, issued the EPA Risk Characterization Policy and Guidance. This policy and guidance is intended to ensure that characterization information from each stage of a risk assessment is used in forming conclusions about risk and that this information is communicated from risk assessors to risk managers, and from EPA to the public. The policy also provides the basis for greater clarity, transparency, reasonableness, and consistency in risk assessments across EPA programs. The fundamental principles which form the basis for a risk characterization are as follows:

- Risk assessments should be transparent, in that the conclusions drawn from the science are identified separately from policy judgments, and the use of default values or methods and the use of assumptions in the risk assessment are clearly articulated.

- Risk characterizations should include a summary of the key issues and conclusions of each of the other components of the risk assessments, as well as describe the likelihood of harm. The summary should include a description of the overall strengths and limitations (including uncertainties) of the assessment and conclusions.

- Risk characterizations should be consistent in general format, but recognize the unique characteristics of each specific situation.

- Risk characterizations should include, at least in a qualitative sense, a discussion of how a specific risk and its context compares with similar risks. This may be accomplished by comparisons with other chemicals or situations on which the Agency has decided to act, or other situations with which the public may be familiar. The discussion should highlight the limitations of such comparisons.

- Risk characterization is a key component of risk communication, which is an interactive process involving exchange of information and expert opinion among individuals, groups, and institutions.

2. Additional Guiding Principles

- The risk characterization integrates the information from the hazard identification, dose-response, and exposure assessments, using a combination of qualitative information, quantitative information, and information regarding uncertainties.

- The risk characterization includes a discussion of uncertainty and variability.

- Well-balanced risk characterizations present conclusions and information regarding the strengths and limitations of the assessment for other risk assessors, EPA decision-makers, and the public.

3. Risk Characterization Applied to the Revised AWQC Methodology

In developing the methodology presented today, the EPA has closely followed the risk characterization guiding principles listed above. As States and Tribes develop criteria using the revised methodology, they are strongly encouraged to follow EPA's risk characterization guidance. There are a number of areas within the methodology and criteria development process where risk characterization principles apply:

- Integration of cancer and noncancer assessments with exposure assessments, including bioaccumulation potential determinations, in essence, weighing the strengths and weaknesses of the risk assessment as a whole when developing a criterion.

- Selecting a fish consumption rate, locally derived or default value, within the context of a target population (e.g., sensitive subpopulations) as compared to the general population.

- Presenting cancer and/or noncancer risk assessment options.

- Describing the uncertainty and variability in both the hazard identification, the dose-response and the exposure assessment.

(a) Health Risks to Children

In recognition that children have a special vulnerability to many toxic substances, Administrator Carol Browner directed EPA in 1995 to explicitly and consistently take into account environmental health risks to infants and children in all risk assessments, risk characterizations and public health standards set for the United States. In April 1997, President Clinton signed Executive Order 13045 on the protection of children from environmental health risks, which assigned a high priority to addressing risks to children. In May 1997, EPA established the Office of Children's Health Protection to ensure the implementation of the President's Executive Order. Circumstances where risks to children should be considered in the context of the AWQC Methodology, along with specific recommendations, are discussed in relevant sections throughout this proposal.

Details on risk characterization and the guiding principles stated above are included in to the March 21, 1995 policy statement and the discussion of risk characterization which accompanies the Proposed Guidelines for Carcinogen Risk Assessment 61 FR 17960 (April 23, 1996) and the Reproductive and Toxicity Risk Assessment Guidelines also of 1996 (61 FR 56274).

4. Science, Science Policy, and Risk Management

An important part of risk characterization, as described at the beginning of this Section, is to make risk assessments transparent. This means that conclusions drawn from the science are identified separately from policy judgments and risk management decisions, and that the use of default values or methods, as well as the use of assumptions in risk assessments, are clearly articulated. For the purposes of this revised methodology, EPA will attempt to separate out scientific analysis from science policy and risk management decisions. This will ultimately allow the States

and Tribes, and specifically users of this methodology, such as scientists, policy setters, and risk managers, to understand the elements of the methodology accurately and clearly, and to easily separate out the scientific decisions from the science policy and risk management decisions. This is important so that when questions are asked regarding the scientific merit, validity, or apparent stringency or leniency of AWQC, the implementer of the criteria can clearly explain what judgments were made to develop the criterion in question and to what degree these judgments were based on science, science policy, or risk management. To some extent this process will also be displayed in future AWQC documents.

When EPA speaks of science or scientific analysis, we are referring to the extraction of data from either toxicological or exposure studies and surveys with a minimum of judgment being used to make inferences from the available evidence. For example, if we are describing a point of departure from an animal study (e.g., a lowest-observed-adverse-effect level, or LOAEL), this is usually determined as a lowest dose which produces an observable adverse effect. This would constitute a scientific determination. Judgments applying science policy, however, may enter this determination. For example, several scientists may differ in their opinion of what is adverse, and this in turn can influence the selection of a LOAEL in a given study. The use of an animal study to predict effects in a human in the absence of human data is an inherent science policy decision. The selection of specific uncertainty factors when developing a reference dose is another example of science policy. In any risk assessment, a number of decision points occur where risk to humans can only be inferred from the available evidence. Both scientific judgments and policy choices may be involved in selecting from among several possible inferential bridges when conducting a risk assessment.

Risk management is the process of weighing policy alternatives and selecting the most appropriate regulatory action, integrating the results of risk assessment with engineering data and with social, economic, and political concerns to reach a decision. In this methodology, the choice of a default fish consumption rate which is protective of 90 percent of the general population is a risk management decision. The choice of an acceptable cancer risk by a State or Tribe is a risk management decision.

Many of the parameters in the revised methodology are an amalgam of science, science policy, and/or risk management. For example, most of the defaults chosen by EPA are based on the examination of scientific data and the application of either science policy or risk management. This includes the default assumptions of 2 liters a day of drinking water; the assumption of 70 kilograms for an adult body weight; the use of default percent lipid and particulate organic carbon/dissolved organic carbon (POC/DOC) for developing national BAFs; the default fish consumption rates for the general population and sport and subsistence anglers; the choice of a default cancer risk level. Some decisions are more heavily steeped in science and science policy, such as the choice of default BAFs, and others are more obviously risk management decisions, such as the determination of default fish consumption rates and cancer risk levels. Throughout the revised methodology, EPA has identified just what kind of decision was necessary to develop defaults and what the basis for the decision was. More details on the concepts of science analysis, science policy, risk management and how they are introduced into risk assessments are included in *Risk Assessment in the Federal Government: Managing the Process*, National Academy Press. 1983.

5. Discussion of Uncertainty

(a) Observed Range of Toxicity Versus Range of Environmental Exposure

When characterizing a risk assessment, an important distinction to make is between the observed range of adverse effects (from an epidemiology or animal study) and the environmentally observed range of exposure (or anticipated human exposure) to the contaminant. In many cases, EPA intends to apply a number of default factors to account for uncertainties or incomplete knowledge in developing RfDs or nonlinear cancer risk assessments to provide a margin of protection. In reality, the actual effect level and the environmental exposure levels may be separated by several orders of magnitude. The difference between some observed response and the anticipated human exposure should be described by risk assessors and managers, especially when comparing criteria to environmental levels of a contaminant.

(b) Continuum of Preferred Data/Use of Defaults

In both toxicological and exposure assessments, EPA has defined a continuum of preferred data ranging from a highest preference of chronic human data for toxicological assessments (e.g., studies that examine a long-term exposure of humans to a chemical, usually from occupational and/or residential exposure); and actual field data for many of the exposure decisions that need to be made (e.g., locally derived fish consumption rates, waterbody-specific bioaccumulation rates); to default values which are at the lower end of the preference continuum. EPA has supplied default values for all of the risk assessment parameters in the revised methodology; however, it is important

to note that when default values are used, the uncertainty in the final risk assessment is usually higher, and the final resulting criterion may not be as applicable to local conditions, than is a risk assessment derived from human/field data. Using defaults assumes generalized conditions and may not capture the actual variability in the population (e.g., sensitive subpopulations/high-end consumers). If defaults are chosen as the basis for criteria, these inherent uncertainties should be communicated to the risk manager and the public. While this continuum is an expression of preference on the part of EPA, it does not imply in any way that any of the choices are unacceptable or scientifically indefensible.

(c) Significant Figures

The number of significant figures in a numeric value is the number of certain digits plus one estimated digit. Digits should not be confused with decimal places. For example, 15.1, .0151, and .0150 all have 3 significant figures. Decimal places may have been used to maintain the correct number of significant figures, but in themselves they do not indicate significant figures (Brinker, 1984). Since the number of significant figures must include only one estimated digit, the sources of input parameters (e.g., fish consumption and water consumption rates) should be checked to determine the number of significant figures associated with data they provide. However, the original measured values may not be available to determine the number of significant figures in the input parameters. In these situations, EPA recommends utilizing the data as presented.

When developing criteria, EPA recommends rounding the number of significant figures at the end of the criterion calculation to the same number of significant figures in the least precise

parameter. This is a generally accepted practice which can be found described in greater detail in APHA, 1992 and Brinker, 1984. The general rule is that for multiplication or division, the resulting value should not possess any more significant figures than is associated with the factor in the calculation with the least precision. When numbers are added or subtracted, the number that has the fewest decimal places, not necessarily the fewest significant figures, puts the limit on the number of places that justifiably may be carried in the sum or difference. Rounding off a number is the process of dropping one or more digits so that the value contains only those digits that are significant or necessary in subsequent computations (Brinker, 1984). The following rounding procedures are recommended: 1) if the digit 6, 7, 8, or 9 is dropped, increase the preceding digit by one unit; 2) if the digit 0, 1, 2, 3, or 4 is dropped, do not alter the preceding digit; and 3) if the digit 5 is dropped, round off the preceding digit to the nearest even number (e.g., 2.25 becomes 2.2 and 2.35 becomes 2.4) (APHA, 1992 and Brinker, 1984).

EPA recommends that calculations of water quality criteria be performed without rounding of intermediate step values. The resulting criterion may be rounded to a manageable number of decimal places. However, in no case should the number of digits presented exceed the number of significant figures implied in the data and calculations performed on them. The term "intermediate step values" refers to values of the parameters in Equations ID-1 through ID-3. The final step is considered the resulting AWQC. Although AWQC are, in turn, used for purposes of establishing WQBELs in NPDES permits, calculating TMDLs, and with Superfund ARARs, they are considered the final step of this methodology and, for the purpose of this discussion, where the rounding should occur.

The determination of appropriate significant figures inevitably involves some judgment regarding the fact that some of the equation parameters are adopted default exposure values. Specifically, the default drinking water intake rate of 2 L/day is a value adopted to represent a majority of the population over the course of a lifetime. Although supported by drinking water consumption survey data, this value was adopted as a policy decision and, as such, does not have to be considered in determining the parameter with the least precision. That is, the resulting AWQC need not always be reduced to one significant digit. Similarly, the 70-kg adult body weight has been adopted Agency-wide and represents a default policy decision.

The following example illustrates the rule described above. The example is for hexachlorobutadiene (HCBD), the revised criterion summarized in Appendix VI. The parameters that were calculated (i.e., not policy adopted values) include values with significant figures of two (the Pdp and RSC), three (the SF), and four (the FI and BAF). Based on the revised methodology, the final criterion should be rounded to two significant figures. The bold numbers in parentheses indicate the number of significant figures and those with asterisks also indicate Agency adopted policy values.

$$AWQC = \frac{Pdp}{SF} \cdot RSC \cdot \left(\frac{BW}{DI+(FI \cdot BAF)} \right) \qquad \text{(Equation ID-2)}$$

Example (refer to HCBD document for details on the data):

$$AWQC = \left(\frac{0.054(2)}{300(3)} - 1.2 \times 10^{-4}(2) \right) \times \left(\frac{70(2^{*})}{2(1^{*}) + (0.01780(4) \times 3{,}180(4))} \right)$$

$$AWQC = 7.2 \times 10^{-5} \text{ mg/L } (0.072 \ \mu\text{g/L, rounded from } 7.167 \times 10^{-2} \ \mu\text{g/L})$$

* represents Agency adopted policy value

A number of the values used in the equation may result in intermediate step values that have more than four figures past the decimal place and may be carried throughout the equation. However, carrying more than four figures past the decimal place (equivalent to the most precise parameter) is unnecessary as it has no effect on the resulting criterion calculation.

References

APHA. American Public Health Association. 1992. Standard Methods: For the Examination of Water and Wastewater. 18th Edition. Prepared and published jointly by: American Public Health Association, American Water Works Association, and Water Environment Federation. Washington, D.C.

Brinker, R.C. 1984. Elementary Surveying. 7th Edition. Cliff Robichaud and Robert Greiner, Eds. Harper and Row Publishers, Inc. New York, NY.

Appendix II. Implementation of AWQC Methodology Revisions

Today's Draft AWQC Methodology Revisions raise several important implementation issues. These include the following: (1) the relationship of the 304(a) criteria revisions to other EPA water quality standards activities; (2) the status of existing 304(a) criteria once any revisions to the criteria and the associated methodologies are finalized; (3) the role of States and Tribes in developing the criteria; (4) the appropriateness of EPA revising 304(a) criteria on the basis of a change in one, or fewer than all, parameters; (5) the process EPA will utilize in developing new criteria for additional chemicals and revising existing criteria; and (6) the development of a priority setting process for selecting appropriate 304(a) criteria for revising. Each of these areas is discussed below.

A. Relationship to Other EPA Activities

New information leads to new insights as to how a chemical induces a toxic effect. In response to such new information, EPA continually updates RfDs and dose-response information in IRIS. Toxicity information and exposure assumptions change as additional data become available. This ongoing evolution effects two important and interrelated responsibilities of the Agency, which are carried out concurrently. First, from time to time EPA recalculates the 304(a) water quality criteria to reflect the latest data. These recalculations have been compiled in a series of guidance documents: the Green Book in 1968, the Blue Book in 1972, the Red Book in 1976, and the Gold Book in 1986. The second responsibility pertains to the requirements of Section 303(c).

As part of the water quality standards triennial review process defined in Section 303(c)(1), the States and Tribes are responsible for maintaining and revising water quality standards. Section 303(c)(1) requires States and Tribes to review, and modify if appropriate, their water quality standards at least once every three years. When a State or Tribe fails to revise or adopt water quality standards consistent with the requirements of the CWA, Section 303(c)(4) authorizes EPA to promulgate replacement water quality standards for them. From time to time, EPA has undertaken such promulgations and calculated numeric water quality criteria for the purposes of the Act. In doing so, EPA utilizes the most current available scientific information, such as toxicity data and exposure assumptions.

With the promulgation of Federal criteria under 303(c)(4) and the publication of new or revised 304(a) criteria, the criteria in an early Federal action may differ from the criteria in a subsequent Federal action. Some confusion has arisen among the public with regard to what EPA's current recommended 304(a) water quality criteria are for a given chemical at any given time.

The most recent Federal action establishes the Agency's current water quality criteria. To date, the most recent Federal recalculation of 304(a) criteria occurred in the CTR, not withstanding the fact the CTR was proposed pursuant to Section 303(c)(4) of the Act. (See discussion below.) Again, EPA views the criteria program as constantly evolving. When the AWQC Methodology Revisions are final, any chemical-specific 304(a) criteria published using the revised methodology will be considered the Agency's most current 304(a) criteria. EPA notes revisions of existing 304(a) criteria prior to the finalization of the revised methodology may be undertaken and are not precluded.

As discussed in Appendix I, Section B.3., States and Tribes have three options when adopting water quality criteria for which EPA has published 304(a) criteria. They can establish numerical values based on 304(a) criteria, 304(a) criteria modified to reflect site specific conditions, or other scientifically defensible methods. When States or Tribes revise their water quality criteria to correct deficiencies identified in a Federal promulgation, EPA will assess the scientific defensibility of the criteria in terms of the Agency's most recent recommended water quality criteria. Thus, there may be cases where applicable policies and science have evolved such that EPA would be evaluating the scientific defensibility of State or Tribal criteria, adopted using one of the three options discussed above, on the basis of new information. Furthermore, EPA views Federal 303(c)(4) promulgations as temporary corrections of deficiencies in State and Tribal water quality standards. The triennial review process provides States and Tribes with a process for addressing these deficiencies. Since CWA Section 303(c)(1) requires States and Tribes to review and modify their water quality standards at least once every three years, EPA does not expect or intend to assume the State and Tribal responsibility of periodically reviewing and revising water quality standards, including water quality criteria, through federal promulgations.

EPA developed and published final Water Quality Guidance for the Great Lakes System (the Guidance), codified at 40 CFR part 132, in March 1995 (58 FR 15366). The Guidance consists of water quality criteria for 29 pollutants to protect aquatic life, wildlife, and human health, and detailed methodologies to develop criteria for additional pollutants, implementation procedures, and antidegradation policies and procedures tailored to the Great Lakes system. The Guidance was developed using the best available science, and reflects the unique nature of the Great Lakes ecosystem. Great Lakes States and Tribes are to use the water quality criteria, methodologies,

policies and procedures in the Guidance to establish consistent, enforceable, long-term protection for the waters of the Great Lakes system. Under the CWA, the Great Lakes States are to adopt provisions into their water quality standards and National Pollutant Discharge Elimination System (NPDES) permit programs by March 1997 that are consistent with the Guidance. The Guidance promotes consistency in standards and implementation procedures while allowing appropriate flexibility to States and Tribes to develop equitable strategies to control pollution sources and to promote pollution prevention practices. Today's Draft AWQC Methodology Revisions are being undertaken pursuant to Section 304 of the CWA, is independent of, and does not supersede, the Guidance.

Although consistency in State water quality standards programs is an important goal for EPA, EPA also recognizes it is necessary to provide appropriate flexibility to States and Tribes, both Great Lakes States and non-Great Lakes States, in the development and implementation of place-based water quality programs. In overseeing States' implementation of the CWA, EPA has found that reasonable flexibility is not only necessary to accommodate site-specific conditions and unforseen circumstances, but also to enable innovations and improvements as new approaches and information become available. Recognition of a general need for flexibility is not incompatible with the requirements for the Great Lakes States and Tribes established at Section 118(c)(2). Once States and Tribes have adopted provisions consistent with the Guidance, EPA intends to extend to them flexibility in utilizing new data and information in developing and updating water quality criteria using the Great Lakes Water Quality Guidance methodologies. In the event a Great Lakes State or Tribe fails to adopt provisions consistent with the Guidance, EPA will promulgate provisions consistent with 40 CFR part 132 that will apply to waters and discharges within that jurisdiction.

In the Draft AWQC Methodology Revisions, EPA is presenting the acceptable lifetime cancer risk for the general population in the range of 10^{-5} to 10^{-6} as opposed to the previous range of 10^{-5} to 10^{-7}. The Draft AWQC Methodology also provides that States and Tribes should ensure the most highly exposed populations do not exceed a 10^{-4} risk level. EPA emphasizes selection of a risk level is a component used in the derivation of water quality criteria, and is thus subject to EPA review under Section 303(c) of the CWA. These proposed revisions are consistent with current program office guidance and Agency regulatory actions.

The three criteria summary documents in Appendices IV through VI were derived using a 10^{-6} risk level, which the Agency believes reflects an appropriate risk for the general population. This risk level is already used by many States and Tribes. EPA intends to continue to derive 304(a) criteria at the 10^{-6} risk level, applying a risk management policy which ensures protection for all exposed population groups. EPA acknowledges that at any given risk level for the general population, those segments of the population that are more highly exposed face a higher relative risk. For example, if fish are contaminated at a level permitted by criteria derived on the basis of a risk level of 10^{-6}, individuals consuming up to 10 times the assumed fish consumption rate would still be protected at a 10^{-5} risk level. States and Tribes have the flexibility to adopt water quality criteria that result in a higher risk level (e.g., 10^{-5}). EPA expects to approve such criteria if the State or Tribe has identified the most highly exposed subpopulation within the State or Tribe, demonstrates the chosen risk level is adequately protective of the most highly exposed subpopulation and has completed all necessary public participation. EPA notes that concerns regarding highly exposed subpopulations make it unlikely EPA would approve a State-wide 10^{-4} risk level, unless it was demonstrated that the potentially highly exposed subpopulations are, in fact, not experiencing higher

exposures than the general population. In effect, risk for such subpopulations would not exceed a 10^{-4} risk level. EPA further notes that risk levels and criteria need to be protective of tribal rights under federal law (e.g., fishing, hunting, or gathering rights) that are related to water quality. Such rights may raise unique issues and will need to be evaluated on a case-by-case basis.

B. Status of Existing 304(a)Criteria for Priority Pollutants and Methodology

In November 1980, EPA published criteria development guidelines for the protection of human health, along with criteria for 64 toxic pollutants and pollutant classes (45 FR 79318). The total number of human health criteria published in 1980 was 105. Subsequently, three volatile chemicals (dichlorodifluoromethane, trichlorofluoromethane, and bis-(chloromethyl)-ether) were removed from the priority list. In 1984, the criteria for dioxin were published; this resulted in a total of 103 criteria. In 1986, EPA summarized the available criteria information in Quality Criteria for Water 1986 (1986 "Gold Book"). The 103 human health criteria for the protection of human health were included in the proposed NTR in November 1991 (56 FR 58420). At that time, 83 of the 103 criteria were revised to reflect the contemporary IRIS values. The final NTR (codified at 40 CFR 131.36(b)(1)) included 91 human health 304(a) criteria. Nine previously published criteria were not included in the NTR for the purposes of promulgating federal water quality under 303(c), but remain in effect as published 304(a) criteria. Previously published criteria for seven pollutants were withdrawn in the NTR. The NTR directed permit authorities to specifically address five other pollutants in NPDES permit actions using the States' existing narrative "free from toxicity" criteria. In August, 1997, EPA included revised human health criteria for 22 pollutants in the CTR (62 FR 42160). These 22 criteria, plus the previously published 78 criteria, are the Agency's recommended

human health criteria. As such, they will continue to be used as the basis for Agency decisions, both regulatory and nonregulatory, until EPA revises and reissues chemical-specific criteria. For example, EPA intends to use these criteria: (1) as guidance to States and Tribes for use in establishing water quality standards; (2) as the basis for EPA promulgation of water quality standards; (3) in establishing NPDES water quality-based permit limits, where the criteria have been adopted by a State or Tribe or promulgated by EPA; and (4) for all other purposes of Section 304(a) criteria under the Act. It is important to emphasize again two distinct purposes which are served by the 304(a)criteria. The first is as **guidance** to the States and Tribes in the development and adoption of water quality criteria which will protect designated uses, and the second is as the basis for **promulgation** of a superseding Federal rule when such action is necessary.

As stated above, until such time as EPA re-evaluates a chemical, subjects the criteria to appropriate peer review, and subsequently publishes a revised chemical-specific 304(a) criteria, the existing 304(a) criteria remain in effect. While the Draft AWQC Methodology Revisions represent improvements to the 1980 methodology, EPA believes the 1980 human health 304(a) criteria methodology and the resulting criteria are fundamentally sound from a scientific standpoint. In the Draft AWQC Methodology Revisions, EPA is presenting for public review and comment the latest advancements in risk and exposure assessment and the application of the most recent data available. In this manner, the Agency will continue to strengthen the scientific and technical foundations of the Agency's human health 304(a) criteria and provide an incremental improvement in the level of protection afforded to the public.

EPA has long supported this position. For example, while undertaking reassessments of dioxin, PCBs, and other chemicals, EPA has consistently upheld the use of the current 304(a) criteria for these chemicals and has maintained their scientific acceptability on the grounds that until such time as a reassessment is completed, the existing 304(a) criteria represent EPA's best assessment for that particular chemical.

C. State and Tribal Criteria Development

In keeping with their primary responsibility in establishing water quality standards, EPA encourages States and Tribes to develop and adopt water quality criteria which reflect local and regional conditions by using the options discussed above. States and Tribes will have access to EPA regional, laboratory, and headquarters staff when help is needed for interpretation of the methodology revisions, and for making critical risk assessment decisions. However, when establishing a numerical value based on 304(a) criteria modified to reflect site specific conditions, or on other scientifically defensible methods, EPA strongly cautions States and Tribes not to selectively apply data in order to ensure a water quality criteria which is less stringent than EPA's 304(a) criteria. Such an approach would inaccurately characterize risk in particular.

Once revisions to the human health methodology are finalized, EPA intends to continue to update a limited number of 304(a) criteria per year, developing the toxicological and exposure data needed to conduct risk assessments associated with many of the toxic pollutants covered by the current universe of 304(a) criteria. As discussed below in Section D, updating the exposure factors used in deriving a criterion is not as time- and resource-intensive as completing the toxicological

evaluation. EPA intends to update a limited number of 304(a) criteria each year over the next several years using new national default exposure assumptions, national default BAFs, and updated toxicological values (i.e., new or revised RfDs, cancer dose-response assessments). In establishing water quality criteria, States and Tribes are urged to continue to use the IRIS noncancer and cancer risk assessments, but to adjust the exposure assumptions (e.g., fish consumption and relative source contribution) to account for local and regional conditions. If a State- or waterbody-specific exposure analysis cannot be conducted, States and Tribes should rely on EPA national defaults.

Generally, EPA has sought to conduct re-evaluations of all of the components of each of the 304(a) criteria before revising the criteria. However in recent years, in recognition of both time and resource limitations, EPA has revised existing 304(a) criteria on the basis of a limited number of components for which there are new data or improved science is a reasonable and efficient means to: (1) implement the latest advances in scientific information and Agency policy for exposure analysis; and (2) publish revised 304(a) criteria on a more frequent basis. This approach promotes up-to-date and robust 304(a) criteria.

Once new or revised 304(a) criteria are published by EPA, the Agency expects States and Tribes to adopt new or revised water quality criteria into their water quality standards consistent with the three options discussed above. EPA believes State and Tribal adoption of up-to-date water quality criteria for all pollutants for which EPA has published 304(a) criteria is important for ensuring full and complete protection of human health. EPA emphasizes it will be reviewing State and Tribal water quality standards to assess the need for new or revised water quality criteria. EPA believes five years from the date of publication of new or revised 304(a) criteria is a reasonable time

frame by which States and Tribes should take action. This period is intended to accommodate those States and Tribes which have begun a triennial review and wish to complete the actions they have underway, deferring initiating adoption of new or revised water quality criteria until the next triennial review.

D. Process for Developing New or Revised 304(a) Criteria

Section 304(a)(1) directs the Agency to "develop and publish . . . and from time to time . . . revise criteria for water quality accurately reflecting the latest scientific knowledge." Recent changes in Agency policies and procedures, as well as potential future changes, have implications for 304(a) criteria. These include IRIS updates, the proposed revisions to the cancer risk assessment guidelines, and revisions to the human health criteria methodology such as those in today's Notice. Additionally, when supported by additional scientific information, EPA has approved site-specific and chemical-specific decisions which differ from the 304(a) criteria published in the Gold Book. This situation, as well as the need for Federal promulgations of water quality standards under Section 303(c)(4) discussed above, has led to confusion among States, Tribes, and the public as to the process for developing 304(a) criteria.

Several steps need to occur before a new 304(a) criterion for a chemical is developed or an existing 304(a) criterion is revised. First, new data must be evaluated by appropriate EPA Offices, calculations of a new criterion or any revisions to existing criteria must be completed, and any implications to other EPA programs must be determined. EPA estimates the time to conduct risk assessment ranges from a few months to a year or more. For exposure analyses, EPA estimates the

time to be much shorter, ranging from a few weeks to a few months. EPA's experience is that toxicological evaluations take longer to complete than exposure assessments due the degree and complexity of the analysis. EPA will utilize new, relevant data in calculating a revised criterion value without regard to whether the revised criterion is more or less stringent. As noted above, EPA may revise 304(a) criteria on the basis of one or more components (e.g., BAF, fish intake, toxicity assessment), rather than a full set of components. This approach is in keeping with the Agency's ongoing efforts to strengthen the scientific and technical foundations of the 304(a) criteria.

Second, EPA policy is to subject derivations of new criteria or revisions of existing criteria to appropriate peer review. Agency peer review consists of a documented critical review by qualified individuals or organizations who are independent of those who originally performed the work, but who are collectively equivalent in technical expertise to them. Conducting peer review will help ensure the criteria are technically adequate, appropriately derived, properly documented and satisfy quality requirements. In addition, EPA will accept data and information from interested members of the public during the peer review process. Through peer review of 304(a) criteria, EPA will provide a sound basis for its decisions, enhancing both the credibility and acceptance of the 304(a) criteria.

Finally, EPA publishes criteria and announces their availability in the *Federal Register*. While the process for developing a new 304(a) criterion is basically the same as for revising an existing criterion, the time and resources for developing the necessary data bases for new criteria are significantly greater. However, the criteria development process described above is essentially the same whether undertaken pursuant to 304(a) or 303(c)(4).

In an effort to keep the States, Tribes, and public apprised of the most current Agency information, EPA intends to publish on a regular basis the current recommended 304(a) criteria, and the individual component values used in their derivation, for guidance to States and Tribes in adopting water quality standards under Section 303. Traditionally, EPA has published criteria documents or summaries of these documents (e.g., the Gold Book) as the process for incorporating the latest scientific knowledge and updating 304(a) criteria. Under this new approach, EPA expects to publish annually in the *Federal Register* a table, similar to the one EPA publishes for the drinking water MCLs and Health Advisories, entitled Drinking Water Regulations and Health Advisories (EPA 822-B-96-002). The drinking water matrix includes information on the existing MCLs, MCLGs, health advisories including the RfD, and the cancer assessment for the chemical. The AWQC table will contain all current recommended human health and aquatic life 304(a) criteria values. This table will only include water quality criteria of general national applicability. Water quality criteria derived to address a site specific or watershed situation will not be included. Water quality criteria from proposed or promulgated Federal water quality standards or new or revised 304(a) criteria documents will be regularly incorporated into the table. Additionally, for easier public access, EPA intends to maintain this repository of current EPA 304(a) criteria and supporting information on the Internet on EPA's home pages on the World Wide Web (www.epa.gov).

E. Development of Future Criteria Documents

The Agency intends to implement a streamlined approach to developing criteria documents which focuses on critical toxicological and exposure related studies. This is a departure from the past format in which all existing toxicological and exposure studies were presented in the 1980

criteria documents, with equal emphasis placed on exposure, pharmacokinetics, toxicological effects, and criterion formulation. Due to limited resources and a need to revise and update criteria more frequently, future criteria documents will be more abbreviated, with an emphasis on using current risk assessments (on IRIS or other EPA health assessment documents) where available and focusing to a greater extent on critical exposure and toxicological studies which may influence the development of a 304(a) criterion (e.g., critical effects studies which form the basis of RfD development or cancer assessment). EPA will still review the literature for the latest studies, but does not intend to provide an exhaustive amount of information for those areas which are deemed less significant in the criterion development process. Where there is a significant amount of literature on an area of study (for instance, pharmacokinetics), EPA expects to reference the information or cite existing IRIS support documents which discuss the information in greater detail.

The overall objective of this change in approach is to allow EPA to revise and update 304(a) criteria more frequently, while still maintaining the scientific rigor which EPA requires. With this new format, EPA estimates it can revise several criteria for the same cost as revising a single criterion under the old format.

In Appendices IV through VI of today's Notice, EPA is publishing summaries of revised criteria for three chemicals using the Draft AWQC Methodology Revisions; the full criteria documents are available on EPA's Internet web site at: http://www.epa.gov/OST/Rules. The three chemicals for which criteria have been developed are: acrylonitrile, 1,3-dichloropropene, and hexachlorobutadiene.

1. **Acrylonitrile:** The revised criterion for protection of human health from the consumption of drinking water and organisms is 0.055 μg/L. The criterion for the protection of human health from the consumption of organisms and incidental ingestion of water is 4.0 μg/L. These values are based on an assumed risk level of 1 x 10^{-6}. For more details on assumed parameters in this calculation, see the summary in Appendix IV of this Notice. The complete criteria document is available through NTIS or on EPA's Internet web site.

2. **1,3-Dichloropropene:** The revised criterion for protection of human health from the consumption of drinking water and organisms is 0.34 μg/L. The criterion for the protection of human health from the consumption of organisms and incidental ingestion of water is 14 μg/L. These values are based on an assumed risk level of 1 x 10^{-6}. For more details on assumed parameters in this calculation, see the summary in Appendix V of this Notice. The complete criteria document is available through NTIS or EPA's Internet web site.

3. **Hexachlorobutadiene:** The revised criteria were derived using a nonlinear (MOE) approach. However, both linear and nonlinear approaches are demonstrated for this chemical. Using the linear approach, the criterion for protection of human health from the consumption of drinking water and organisms is 0.046 μg/L (assumed risk level of 1 x 10^{-6}); and the criterion for the protection of human health from the consumption of organisms and incidental ingestion of water is 0.049 μg/L. Using the nonlinear approach, the criterion for protection of human health from the consumption of drinking water and organisms is 0.11 μg/L; and the criterion for the protection of human health from the consumption of organisms and incidental ingestion of water is 0.12μg/L. Again, EPA recommends the nonlinear approach based on the fact that in this specific case, there

is too much uncertainty and not enough confidence using the tumor data (only one data point at a very high dose where the MTD has been exceeded and toxicity is severe) to do a linear high to low dose extrapolation for the estimation of human risk. Moreover, since data from both rats and mice support the same NOAEL value, there is greater confidence in the data base for a nonlinear approach. For more details on assumed parameters in this calculation, see the summary in Appendix VI of this Notice. The complete criteria document is available through NTIS or on EPA's Internet web site.

F. Prioritization Scheme for Selecting Chemicals for Updating

As discussed above, the Agency does not have the resources to immediately develop human health criteria, either new or revised, for all the contaminants found in surface water. Because of this, EPA is soliciting comment on how to prioritize chemicals for future recommended 304(a) criteria using the revised human health methodology. One approach for prioritizing chemicals is for EPA to publish on an annual basis in the *Federal Register* a list of substances for which EPA plans to initiate criterion development or updating. The *Federal Register* Notice would provide the status of any ongoing criteria updates or developments of new criteria. EPA would also ask the public for candidates for new or updated recommended AWQC and would ask for scientific data (either toxicological or exposure related) or a compelling reason(s) to revise a current criterion or develop a new AWQC. This process would be similar to that used by EPA to announce its lists of agents for which cancer hazard and dose-response assessments will be initiated on an annual basis (61 FR 32799). Using the information submitted from the public and other data, the Agency would establish a list of chemicals for which it will initiate work, on an annual basis. EPA intends to maintain an

open docket on the Internet which would allow the public and/or interested parties to review external submissions to the Agency for given chemicals and would also allow an exchange of pertinent information between the public and the Agency.

To initiate this process for prioritization, EPA evaluated chemicals to generate a preliminary list of candidates for revision. Focusing on chemicals that pose the greatest potential risk to human health, the initial universe considered by EPA included the 126 priority pollutants designated as toxic under Section 307(a) of the Act, plus seven additional pollutants included because of their bioaccumulation potential. (EPA was required to publish criteria documents for 65 pollutants and pollutant classes which Congress, in the 1977 amendments to the Clean Water Act, designated as toxic under Section 307(a)(1). The 65 pollutants and pollutant classes were, in total, 129 chemicals which became known as the list of 129 priority pollutants. The final number became 126 when 3 priority pollutants were subsequently deleted.) After careful consideration, EPA identified 98 chemicals as possible candidates for new or revised 304(a) criteria. The 98 chemicals were selected based on the following factors:

- The NTR promulgated 304(a) human health criteria for 91 chemicals. EPA considers these 91 chemicals as a good representation of the priority pollutants for which sufficient data exist to revise 304(a) criteria. (The NTR did not include human health criteria for 35 priority pollutants for the reasons discussed in the final NTR.)

- Seven chemicals for which human health criteria were not developed in the NTR but which have a high potential for bioaccumulation, based on information contained in

the recently promulgated Great Lakes Water Quality Guidance (hexachlorocyclohexane, mirex, octachlorostyrene, pentachlorobenzene, photomirex, 1,2,3,4 tetrachlorobenzene, 1,2,3,5-tetrachlorobenzene).

In prioritizing the 98 chemicals discussed above, EPA considered four factors: 1) toxicity data from IRIS; 2) data on occurrence in fish tissue from *The Incidence and Severity of Sediment Contamination in Surface Waters of the United States* (EPA-823-R-97-006), 3) data on the occurrence in sediments from *The Incidence and Severity of Sediment Contamination in Surface Waters of the United States*; and 4) data on BAFs for trophic level 4 from either the proposed or final Great Lakes Water Quality Initiative Guidance (GLWQI or GLI). Of these four factors, EPA selected the potential for bioaccumulation (i.e., BAFs and Log K_{ow}) along with toxicity (i.e., cancer slope factor or RfD) as the most indicative of potential risk to human health. Taking these two factors into consideration, EPA chose 29 chemicals from the list of 98 originally considered. This list provides the initial basis for criteria revision decisions, along with other Agency chemical ranking lists and input from States and Tribes. Furthermore, EPA intends to use these two factors for ranking contaminants in the future. EPA would review these priorities in light of Agency resources and programmatic commitments when making decisions to develop and/or revise 304(a) criteria in the future. New criterion updates and starts would be presented in an annual *Federal Register* Notice, as described in Section D. PCBs, mercury, and dioxin are not on the priority list because EPA is already committed to developing updated AWQC for these chemicals. The 29 highest ranked chemicals out of the 98 considered (not in order of priority) are the following:

Benz(a)-Anthracene 4,4'-DDT

Benzo(a)-Pyrene	4,4'-DDE
4-Bromo-phenyl Phenyl-Ether	4,4'-DDD
4-Chloro-phenyl Phenyl Ether	Dieldrin
Dibenzo(a,h)Anthracene	Endrin
Di-n-Butyl Phthalate	Heptachlor
Hexachloro-benzene	Heptachlor Epoxide
Hexachloro-butadiene	Mirex/dechlorane
Aldrin	Octachlorostyrene
Hexachlorocyclohexane	Pentachlorobenzene
alpha-BHC	Photomirex
beta-BHC	1,2,3,4-Tetrachlorobenzene
gamma-BHC	1,2,3,5-Tetrachlorobenzene
delta-BHC	Toxaphene
Chlordane	

EPA is also planning to review other prioritization efforts within the Agency to consider possible non-bioaccumulative contaminants found in surface water. Specifically, EPA will evaluate the Safe Drinking Water Contaminant List and risk analyses from the Office of Pesticide Programs.

G. Request for Comments

EPA requests comment on all aspects of the implementation strategy and specifically requests comment on the following areas.

1. Because, as a general matter, EPA uses the cancer risk range of 10^{-4} to 10^{-6} when setting criteria and standards, the Agency recommends a consistent approach here (i.e., 10^{-5} to 10^{-6} for the general population, while ensuring that the most highly exposed population does not exceed a risk level of 10^{-4}). EPA requests comment on this recommendation and its intention to derive 304(a) criteria at the 10^{-6} level. Are there other issues that the Agency should consider regarding this policy?

2. Should EPA revise existing 304(a) criteria on the basis of a partially updated data set (e.g., update exposure factors to be used in calculating 304(a) criteria)?

3. With what frequency should new criteria be developed or existing criteria updated? Is annually sufficient?

4. Does the streamlined approach to developing criteria documents appropriately characterize the derivation of criteria using the proposed methodology? Readers are directed to the three criteria documents available through NTIS and EPA's Internet site as examples of this new approach.

5. Is the list of 29 chemicals which EPA selected for prioritization appropriate? What other chemicals should be added to the list, and why should they be added to the list?

Appendix III. Elements of Methodology Revisions and Issues by Technical Area

A. Cancer Effects

1. Background on EPA Cancer Assessment Guidelines

(a) 1980 AWQC National Guidelines

When EPA published the 1980 AWQC National Guideline (USEPA, 1980), 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 (USEPA, 1976). 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 any dose of the carcinogen results in some possibility of a tumor (i.e., a nonthreshold phenomenon).

Under the 1980 guidelines, two types of data are used for quantitative estimates: (1) lifetime animal studies; and (2) human studies where excess cancer risk is associated with exposure to the agent. (Human data with sufficient quantification to carry out risk assessment are generally not available for most agents because there is a lack of exposure data, especially for confounders.) The

scaling of doses from animals to humans uses a conversion factor of body weight to the 2/3 power ($BW^{2/3}$) to approximate the expression of dose in terms of surface area of the target organ (represented as a perfect sphere), with exposure defined in mg of contaminant/(body weight)$^{2/3}$/day[4]. This approach is based on the assumption that equivalent doses between animal species can be expressed in terms of mg/surface area/day (Mantel and Schneiderman, 1975). This assumption is more appropriate at low applied-dose concentrations where sources of nonlinearity, such as saturation or induction of enzyme activity, are less likely to occur.

The estimation of cancer risk to humans typically used animal bioassay data extrapolated to low doses approximating human exposure using the LMS. The LMS model was fit to tumor data using a computer program (e.g., GLOBAL 86) that calculated the 95th percentile upper confidence limit on the linear slope in the low-dose range. The slope that is obtained is referred to as the q_1*, and was used as an estimate of 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 and slope factors derived from other models were expressed in the form of x (mg/kg-day)$^{-1}$ and are often used to estimate the upper bound of the lifetime cancer risk for long-term low-level exposure to agents.

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[4] The specific equation for converting an animal dose to a human equivalent dose using the $BW^{2/3}$ scaling factor is:

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

that is equivalent to

$$\text{Animal Dose} \left(\frac{\text{Animal BW}}{\text{Human BW}}\right)^{1/3}$$

Upper-bound risk assessments carried out with the low-dose linear model were generally considered conservative, representing the most plausible 95th percentile upper bound for risk. The "true risk" was considered unlikely to exceed the risk estimate derived by this procedure, and could be as low as zero at low doses. The use of low-dose linear extrapolation with a default to LMS was endorsed by four agencies in the Interagency Regulatory Liaison Group and was characterized as less likely to underestimate risk at the low doses typical of environmental exposure than other models and approaches that were available. Because of the uncertainties associated with extrapolation from high to low dose and from animals to humans, assumed water and fish exposure, and the serious public health consequences that could result if risk were underestimated, EPA believed that it was prudent to use the LMS to estimate cancer risk for the AWQC. In deriving water quality criteria, the slope factors are currently estimated using the LMS model under most circumstances.

Basic assumptions that are used to calculate the AWQC include a daily consumption rate of 2 liters of water per day (from all sources), a daily fish consumption rate of 6.5 grams per day, and a 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 mg/L for carcinogens presented in the 1980 AWQC National Guidelines is:

$$\text{AWQC (mg/L)} = \frac{(10^{-6})\ (70)}{(q_1^*)(2+0.0065R)} \qquad \text{Equation IIIA-1}$$

where:

10^{-6} = 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 $(mg/kg\text{-}day)^{-1}$

2 = assumed daily water consumption of an adult human (L/day)

0.0065 = assumed daily consumption of fish (kg)

R = bioconcentration factor (L/kg) from water to food (e.g., fish, birds)

(b) 1986 EPA Guidelines for Carcinogenic Risk Assessment

Since 1980, EPA risk assessment practices have evolved significantly. In September 1986, EPA published its Guidelines for Carcinogen Risk Assessment (referred to subsequently in this document as the 1986 Cancer Guidelines) in the *Federal Register* (51 FR 33992) (USEPA, 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 categorize chemicals into alpha-numerical groups: A (known human carcinogen; sufficient evidence from epidemiological studies or other human studies); B (probable human carcinogen; sufficient evidence in animals and limited or inadequate evidence in humans); C (possible human carcinogen; limited evidence of carcinogenicity in animals in the absence of human data); D (not classifiable; inadequate or no animal evidence of carcinogenicity); and E (no evidence of carcinogenicity in at least two adequate species or in both epidemiological and animal studies). Within Group B there are two subgroups, Groups B1 and B2. Group B1 is reserved for agents for which there is limited evidence of carcinogenicity from epidemiological 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 epidemiological studies would usually be categorized under Group B2 (USEPA, 1986). The system was similar to that used by the International Agency for Research on Cancer (IARC).

The 1986 Cancer Guidelines include guidance on what constitutes sufficient, limited, or inadequate evidence. In epidemiological studies, sufficient evidence indicates a causal relationship between the agent and human cancer; limited evidence indicates that a causal relationship is credible, but that alternative explanations, such as chance, bias, or confounding, could not adequately be excluded; inadequate evidence indicates either lack of pertinent data, or a causal interpretation is not credible. In animal studies, sufficient evidence includes an increased incidence of malignant tumors or combined malignant and benign tumors:

a) In multiple species or strains;

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

c) To an unusual degree in a single experiment with regard to high incidence, unusual site or type of tumor, or early age at onset;

d) Additional data on dose-response; short-term tests or structural activity relationship.

Limited evidence includes studies involving a single species, strain, or experiment which do not meet criteria for sufficient evidence; experiments restricted by inadequate dosage levels,

inadequate duration of exposure, inadequate period of follow-up, poor survival, too few animals, or inadequate reporting; an increase in benign but not malignant tumors with an agent showing no response in a variety of short-term tests for mutagenicity; or responses of marginal statistical significance in a tissue known to have a high or variable background rate.

In the 1986 Cancer Guidelines, hazard identification and the weight-of-evidence process focus on tumor findings. The human carcinogenic potential of agents is characterized by a six-category alphanumeric classification system. The weight-of-evidence approach for making judgment about cancer hazard analyzes human and animal tumor data separately, then combines them to make the overall conclusion about potential human carcinogenicity. The next step of the hazard analysis is an evaluation of supporting evidence (e.g., mutagenicity, cell transformation) to determine whether the overall weight-of-evidence conclusion should be modified.

For cancer risk quantification, the 1986 Cancer Guidelines recommend the use of LMS as the only default approach. The 1986 Cancer Guidelines also mention that a low-dose extrapolation model other than the LMS might be considered more appropriate based on biological grounds. However, no guidance was given in choosing other approaches. The 1986 Cancer Guidelines continued to recommend the use of $(BW)^{2/3}$ as a dose scaling factor between species.

(c) 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 feels that the alphanumeric classification scheme for carcinogens adopted in 1986 was too rigid and relied too heavily on tumor findings and the full use of all relevant information, an understanding of how the agent induces tumors, and the relevance of the mode of action to humans was not promoted. Because guidance was not provided in the 1986 Cancer Guidelines for developing a mode of action understanding about how the agent induces tumors, dose-response assessments have been traditionally based on the modeling of tumor data with the LMS approach. There is an increasing number of examples of where the use of linear extrapolation may not be appropriate (e.g., nonmutagenic carcinogens causing a hormonal imbalance and thyroid gland neoplasia, or inducing bladder tumors secondary to bladder calculi-induced hyperplasia). Additionally, the circumstances or conditions under which a particular hazard is expressed (e.g., route, duration, pattern, or magnitude of exposure) are not conveyed with the 1986 letter classification system.

The Office of Water has also reviewed the guidance provided by the 1992 National Workshop on Revision of the Methods for Deriving National Ambient Water Quality Criteria for the Protection of Human Health (USEPA, 1993) and EPA's SAB review of the 1992 National Workshop report on cancer-related issues[5]. As recommended by these two groups, the Office of Water is revising the cancer risk assessment methodology for the development of AWQC by

[5] The 1992 National Workshop on Revision of the Methods for Deriving National Ambient Water Quality Criteria for the Protection of Human Health (USEPA, 1993) and EPA's Scientific Advisory Board (SAB) review of the workshop identified several issues on cancer. EPA was encouraged by both groups to incorporate new approaches into the AWQC methodology. Further, the SAB recommended against the interim adoption of the 1986 Cancer Guidelines into the AWQC methodology, indicating that it might create considerable confusion in the future, once new Cancer Guidelines are formally proposed and implemented.

incorporating principles consistent with the *Proposed Guidelines for Carcinogenic Risk Assessment* dated April 23, 1996 (USEPA, 1996).

2. Proposed Revisions to EPA's Carcinogen Risk Assessment Guidelines

EPA has recently published *Proposed Guidelines for Carcinogen Risk Assessment* (USEPA, 1996), that revise the 1986 Cancer Guidelines. These revisions are designed to ensure that the Agency's cancer risk assessment methods reflect the most current scientific information.[6] Although many fundamental aspects of the current cancer risk assessment approach have been retained, there are a number of key changes proposed, some of which address the specific problems mentioned in the preceding section. Proposed changes to the cancer guidelines are discussed here because many of the changes that are proposed are incorporated into the AWQC methodology in this Notice.

The key changes in the Proposed Cancer Guidelines include:

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).

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

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 3 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 by 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}).[7] The linear default is a straight line extrapolation from the response at 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 determine the appropriate margin between the Pdp and the projected exposure level (i.e., the AWQC). 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) **Refining the approach used to calculate oral human equivalent dose** when assessments are based on animal bioassays including a change in the default assumption for interspecies dose scaling (using body weight raised to the 3/4 power).

[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.

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.

The Notice, 61 FR 17960 April 23, 1996, and its supporting administrative record should be consulted for detailed information (USEPA, 1996).

3. Revised Carcinogen Risk Assessment Methodology for Deriving AWQC[8]

The revised methodology for deriving numerical AWQC for carcinogens incorporates the principles consistent with the Proposed Cancer Guidelines. This discussion of the revised methodology for carcinogens focuses primarily on the quantitative aspects of deriving numerical AWQC values. 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. A numerical AWQC value derived for a carcinogen is to be accompanied by appropriate hazard assessment and risk characterization information.

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[8] Additional information regarding the revised methodology may be found in Ambient Water Quality Criteria Derivation Methodology–Human Health. Technical Support Document. (USEPA, 1998).

This Section contains a discussion of the weight-of-evidence narrative, that describes all information relevant to a cancer risk evaluation, 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: (1) dose estimation; (2) characterizing dose-response relationships in the range of observation and at low, environmentally relevant doses; (3) calculating the AWQC value; (4) risk characterization; and (5) use of toxicity equivalent factors (TEF) and Relative Potency Estimates. The first three listed topics encompass the quantitative aspects of deriving AWQC for carcinogens.

(a) Weight-of-Evidence Narrative[9]

As stated in the EPA Proposed Cancer Guidelines, the new method includes a weight-of-evidence narrative that is based on an overall weight-of-evidence of biological and chemical/physical considerations. Hazard assessment information accompanying an AWQC value for a carcinogen is provided in the form of a weight-of-evidence narrative as described in the footnote. Of particular importance is that the weight-of-evidence narrative explicitly provides adequate support based on

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[9] The weight-of-evidence narrative is intended 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, 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 (USEPA, 1996).

human studies, animal bioassays, and other key evidence for the conclusion that the substance is a "known or likely" human carcinogen from exposures through drinking water and/or fish ingestion. The Agency emphasizes the importance of providing an explicit discussion of the mode of action for the substance in the weight-of-evidence narrative, including a discussion that relates the mode of action to the quantitative procedures used in the derivation of the AWQC.

(b) Dose Estimation

(1) 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 where possible. 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 unit mass per unit body weight per unit time, (e.g., mg/kg-day). When animal bioassay data are used, it is necessary to make adjustments to the applied 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 adequate data are available, the doses used in animal studies can be adjusted to equivalent human doses using toxicokinetic information on the particular agent. 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. To derive an equivalent human oral dose from animal data, the new default procedure is to scale daily applied oral doses experienced for lifetime in proportion to body weight raised to the 3/4 power. The adjustment factor is used because metabolic rates, as well as most rates of physiological processes that determine the disposition of 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 (USEPA, 1996).

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

The use of body weight raised to 3/4 power ($BW^{3/4}$) is a departure from the scaling factor of $BW^{2/3}$, which was based on surface area adjustment and was included in the 1980 AWQC National Guidelines as well as the 1986 Cancer Guidelines. A more extensive discussion of the rationale and data supporting the Agency's adoption of this scaling factor is in USEPA (1992) and the Proposed Cancer Guidelines.

(2) 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 7 days per week.

If, for example, "daily" dosing is done only 5 days each week, the lifetime daily dose would be calculated as 5/7 of the actual dose given on each of the 5 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.

(3) Dose-Response Analysis

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 such as to justify investing resources supporting use, this 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.

(c) 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. 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 response data. It should be noted that the 1996 proposed guidelines call for modeling of not only tumor data in the observable range, but also other responses thought to be important events proceeding tumor development (e.g., DNA adducts, cellular proliferation, receptor binding, hormonal changes). The modeling of these data are intended to better inform the dose-response assessment by providing insights into the relationships of exposure (or dose) and tumor response below the observable range. These nontumor response data can only play a role in the dose-response assessment if the agent's carcinogenic mode of action is reasonably understood, as well as, the role of that precursor event.

The Proposed Cancer Guidelines recommend calculating the lower 95 percent confidence limit on a dose associated with an estimated 10 percent increased tumor or relevant nontumor

response (LED_{10}) for quantitative modeling of dose-response relationships in the observed range. The estimate of the LED_{10} is used as the point of departure for low-dose extrapolations discussed below. The LED_{10}, the lower 95 percent confidence limit on a dose associated with 10 percent extra risk, a standard point of departure, is adopted as a matter of science policy to remain as consistent and comparable from case to case as possible. It is also a convenient comparison point for noncancer endpoints. The rationale supporting use of the LED_{10} is that a 10 percent response is at or just below the limit of sensitivity of 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. The estimate of the LED_{10} involves considerable judgment in dealing with uncertainties related to such factors as selection of approach, number and spacing of doses, sample sizes, the precision and accuracy of dose measurements, and the accuracy of pathological findings.

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—determine the extrapolation range. Therefore, if the observed response is below the LED_{10}, then a lower point may be a better choice (e.g., LED_5). Moreover, some forms of data may not be amenable to curve-fitting estimation, but to estimation of a LOAEL or NOAEL instead, 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.

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

(2) Biologically Based Modeling Approaches

If a biologically based or case-specific modeling approach 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 to environmentally relevant doses. For the

purposes of risk management derivation of AWQC, the environmentally relevant dose would be the RSD associated with incremental lifetime cancer risks in the 10^{-4} to 10^{-6} range for carcinogens on which a linear extrapolation approach is applied.[10] The use of the RSD and the Pdp/SF to compute the AWQC is presented in Appendix II, Section A.3(d), below. 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 the use of such approaches for most substances. In the absence of such data, the default linear approach, the nonlinear (margin of exposure) approach, or both linear and nonlinear approaches will be used.

(3) Default Linear Extrapolation Approach

The default linear approach proposed here is a replacement of the 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 (1) agents with a mode of action of gene mutation due to DNA reactivity; (2) 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 (3) carcinogenic agents lacking information on the mode of action. The proposed default linear approach is considered generally conservative regarding the protection of public health. 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 other information to the contrary.

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[10] For discussion of the cancer risk range, see Appendix II, Section A and Appendix III, Section C.1(a).

The procedures for implementing the default linear approach begin with the estimation of a point of departure as described above. The point of departure, LED_{10}, reflects 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 and the origin (i.e., zero dose, zero extra risk). This is mathematically represented as:

$$y = mx + b \qquad \text{(Equation IIIA-2)}$$

$$b = 0$$

where:

y = Response or incidence

m = Slope of the line (cancer potency factor) = $\frac{\Delta y}{\Delta x}$

x = Dose

b = Slope intercept

The slope of the line, "m" (the estimated cancer potency factor at low doses), is computed as:

$$m = \frac{0.10}{LED_{10}} \qquad \text{(Equation IIIA-3)}$$

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

$$RSD = \frac{\text{Target Incremental Cancer Risk}}{m} \qquad \text{(Equation IIIA-4)}$$

where:

RSD	=	Risk-specific dose (mg/kg-day)
Target Incremental Cancer Risk[11]	=	Value 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 in Section D below.

(4) Default Nonlinear Approach

As discussed in the Proposed Cancer Guidelines, the use of a nonlinear approach for risk assessment is recommended where there is no evidence for linearity and there is sufficient evidence to support an assumption of nonlinearity.

The nonlinear approach is indicated for agents having a mode of action that may lead to a dose-response relationship that is nonlinear, with response falling much more quickly than linearly with dose, or being most influenced by individual differences in sensitivity. The mode of action may

[11] 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. See Appendix I, Section D for more details.

theoretically be nonlinear because of 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).

Mode of action data are used for all cases. The nonlinear approach may be used, for instance, in the case of an organophosphate, where the chemical is not mutagenic and causes only stone formation in male rat bladders at high doses. This dynamic leads to tumor formation only (at the high doses). Stone and subsequent tumor formation are not expected to occur at doses lower than those that induce the physiological changes that lead to stone formation. (More detail on this chemical is provided in the cancer section of the Technical Support Document). EPA does not generally try to distinguish between modes of action that might imply a "true threshold" from others with a nonlinear dose-response relationship, because there is usually not sufficient information to distinguish between these empirically.

The nonlinear margin of exposure (MoE) approach in the Proposed Cancer Guidelines compares an observed response rate such as the LED_{10}, NOAEL, or LOAEL with actual environmental exposures of interest by computing the ratio between the two. In the context of deriving AWQC, the environmentally relevant exposures are targets rather than actual exposures.

If the evidence for an agent indicates a nonlinearity (e.g., when carcinogenicity is secondary to another toxicity for which there is a threshold), the MoE analysis for the toxicity is similar to what is done for a noncancer endpoint, and an RfD or RfC for that toxicity may also be estimated and considered in the cancer assessment. However, a threshold of carcinogenic response is not

necessarily assumed. It should be noted that for cancer assessment, the margin of exposure analysis begins from a point of departure that is adjusted for toxicokinetic differences between species to give a human equivalent dose.

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 that influence the selection of the SF in an MoE approach are included in the discussion.

There are two main steps in the MoE approach. The first step is the selection of a point of departure (Pdp). 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 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 previously in this Notice) or toxicokinetic analysis.

The second step in using MoE analysis to establish AWQC is the selection of an appropriate margin or SF to apply to the Pdp. This is supported by analyses in the MoE discussion in the risk assessment. The following issues should be considered when establishing the overall 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.

(A steeper slope implies a greater reduction in risk as exposure decreases. This 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 of exposure; and

- Persistence of the agent in the body. This is particularly relevant when precursor data from less-than-lifetime studies are the response data being assessed.

As a default assumption for two of these points, the Proposed Cancer Guidelines recommend 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 fraction may be employed to account for this. If information about human variability or interspecies differences is available, it is used.

After considering all the issues together, the risk manager decides on the margin of safety (MoS). The size of the MoS is a matter of policy and is selected on a case-by-case basis, considering the weight-of-evidence and the margin of exposure analysis provided in the risk assessment.[12]

(5) Both Linear and Nonlinear Approaches

In some cases both linear and nonlinear 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 (USEPA, 1996). The use of both the default linear approach and the nonlinear approach may be appropriate to discuss implications of complex dose-response relationships. For example, if it is apparent that an agent is both DNA reactive and is highly active as a promoter at high doses, and there are insufficient data for modeling, both linear and nonlinear default procedures may be needed to decouple and consider the contribution of both phenomena (USEPA, 1996). For further discussion on making risk assessment decisions between these approaches, refer to the Proposed Cancer Guidelines (USEPA, 1996).

[12] Guidance on selecting appropriate safety factors is provided in the Proposed Guidelines for Carcinogenic Risk Assessment (USEPA, 1996).

(d) AWQC Calculation

Linear Approach

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

$$AWQC = RSD \cdot \left(\frac{BW}{DI + (FI \cdot BAF)} \right) \qquad \text{(Equation IIIA-5)}$$

Nonlinear Approach

In those cases where the nonlinear, MoE approach is used, a similar equation is used to calculate the AWQC [13]

$$AWQC = \frac{Pdp}{SF} \cdot RSC \cdot \left(\frac{BW}{DI+(FI \cdot BAF)} \right) \qquad \text{(Equation IIIA-6)}$$

where:

AWQC	=	Ambient water quality criterion (mg/L)
RSD	=	Risk-specific dose (mg/kg-day)
Pdp	=	Point of departure (mg/kg-day)

[13] Although appearing in this equation as a factor to be multiplied, the RSC can also be an amount subtracted.

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 (percentage or subtraction)

A difference between the AWQC values obtained using the linear and nonlinear approaches should be noted. First, 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 obtained using the nonlinear approach does not describe a specific cancer risk.

The AWQC calculations shown above are appropriate for waterbodies that are used as sources of drinking water. If the waterbodies are not used as drinking water sources, the approach is modified. The drinking water value (DI in the equations 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.

The actual AWQC chosen for the protection of human health is based on a review of all relevant information, including cancer and noncancer data. The AWQC may, or may not, utilize the value obtained from the cancer analysis in the final AWQC value. The endpoint selected for the AWQC will be based on consideration of the weight-of-evidence and a complete analysis of all toxicity endpoints.

(e) Risk Characterization

Risk assessment is an integrative process that culminates ultimately into a risk characterization summary. Risk characterization is the final step of the risk assessment process in which all preceding analyses (i.e., hazard, dose–response, and exposure assessments) are tied together to convey the overall conclusions about potential human risk. This component of the risk assessment process characterizes the data in nontechnical terms, explaining the extent and weight-of-evidence, major points of interpretation and rationale, strengths and weaknesses of the evidence, and discusses alternative approaches, conclusions, and uncertainties that deserve serious consideration.

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.

(f) 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 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, according to the Proposed Cancer Guidelines, adequate data to support use of TEFs has been found in only one class of compounds (dioxins) (USEPA, 1989; 1996).

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 potencies 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).

4. Request for Comments

EPA's Office of Water requests comments on the revised methodology in this Notice. Topics on which comment is particularly sought are indicated below. Comments on the Proposed Cancer Guidelines are not solicited here; the comment period on the Proposed Cancer Guidelines ended in August 1996. EPA will reflect changes in the final Cancer Guidelines in the final Human Health methodology. Comments on the application of the concepts and principles of the revised AWQC methodology are relevant and solicited here.

The Agency requests comment on the new approaches to dose-response assessment and modeling described in this Section.

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B. Noncancer Effects

1. 1980 AWQC National Guidelines for Noncancer Effects

In the 1980 AWQC National Guidelines, the Agency evaluated noncancer human health effects from exposure to chemical contaminants using ADI levels. ADIs were calculated by dividing NOAELs by SFs to obtain estimates of doses of chemicals that would not be expected to cause adverse effects over a lifetime of exposure. In accordance with the National Research Council report of 1977 (NAS, 1977), EPA used SFs of 10, 100, or 1,000, depending on the quality and quantity of the overall data base. In general, a factor of 10 was suggested when good-quality data identifying a NOAEL from human studies were available. A factor of 100 was suggested if no human data were

available but the data base contained valid chronic animal data. For chemicals with no human data and scant animal data, a factor of 1,000 was recommended. Intermediate SFs could also be used for data bases that fell between these categories.

AWQC were then calculated using the ADI levels together with standard exposure assumptions about the rates of human ingestion of water and fish, and also accounting for intake from other sources (see Equation IB-1 in the Introduction). Surface water concentrations at or below the calculated criteria concentrations would be expected to result in human exposure levels at or below the ADI. Inherent in these calculations is the assumption that, generally, noncarcinogens exhibit a threshold.

2. Noncancer Risk Assessment Developments Since 1980

Since 1980, the risk assessment of noncarcinogenic chemicals has changed. To remove the value judgments implied by the words "acceptable" and "safety," the ADI and SF terms have been replaced with the terms RfD and UF/modifying factor (MF), respectively.

For the risk assessment of general systemic toxicity, the Agency currently uses the guidelines contained in the IRIS Background Document entitled *Reference Dose (RfD): Description and Use in Health Risk Assessments*. That document 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" (USEPA, 1993a). The most common approach for deriving the RfD does not involve

dose-response modelling. Instead, an RfD for a given chemical is usually derived by first identifying the NOAEL for the most sensitive known toxicity endpoint, that is, the toxic effect that occurs at the lowest dose. This effect is called the critical effect. Factors such as the study methodology, the species of experimental animal, the nature of the toxicity endpoint assessed and its relevance to human effects, the route of exposure, and exposure duration are critically evaluated in order to select the most appropriate NOAEL from among all available studies in the chemical's data base. If no appropriate NOAEL can be identified from any study, then the LOAEL for the critical effect endpoint is used and an uncertainly factor for LOAEL to NOAEL extrapolation is applied. Using this approach, the RfD is equal to the NOAEL (or LOAEL) divided by the product of uncertainty factors and, occasionally, a modifying factor:

$$\text{RfD (mg/kg/day)} = \frac{\text{NOAEL (or LOAEL)}}{\text{UF} \cdot \text{MF}} \qquad \text{(Equation IIIB-1)}$$

The definitions and guidance for use of the uncertainty factors and the modifying factor are provided in the IRIS Background Document and are repeated in Table IIIB-1.

The IRIS Background Document on the Reference Dose (USEPA, 1993a) provides guidance for critically assessing noncarcinogenic effects of chemicals and for deriving the RfD. Another reference on this topic is Dourson (1994). Furthermore, the Agency has also published separate guidelines for assessing specific toxic endpoints, such as developmental toxicity (USEPA, 1991a); reproductive toxicity (USEPA, 1996a); and neurotoxicity risk assessment (USEPA, 1995a). These endpoint-specific guidelines will be used for their respective areas in the hazard assessment step and

will complement the overall toxicological assessment. It should be noted, however, that an RfD, derived using the most sensitive known endpoint, is considered protective against all noncarcinogenic effects.

TABLE IIIB-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 factor of 1, 3, or 10 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 factor of 1, 3, or 10 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 factor of 1, 3, or 10 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 3- or 10-fold factor when deriving an RfD from an "incomplete" data base. This factor is meant to account for the inability of any single type of study to consider all toxic endpoints. The intermediate factor of 3 (approximately ½ $\log_{10}$ unit, i.e., the square root of 10) 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 total product of the uncertainty factors and modifying factor should not exceed 3,000.	

Similar to the procedure used in the 1980 AWQC National Guidelines, the revised derivation of AWQC values for noncarcinogens uses the RfD together with various assumptions concerning intake of the contaminant from both water and nonwater sources of exposure. The objective of the

AWQC value for noncarcinogens is to ensure that human exposure to a substance related to its presence in surface water, combined with exposure from other sources, does not exceed the RfD. The algorithm for deriving AWQC for noncarcinogens using the RfD is presented as Equation ID-1 in the Introduction and discussed further in Appendix II, Section C in this Notice.

3. Issues and Recommendations Concerning the Derivation of AWQC for Noncarcinogens

During a review of the 1980 AWQC National Guidelines (USEPA, 1993b), the Agency identified several issues that must be resolved in order to develop a final revised methodology for deriving AWQC based on noncancer effects. These issues, as discussed below, mainly concern the derivation of the RfD as the basis for such an AWQC value. Foremost among these issues is whether the Agency should revise the present method or adopt entirely new procedures that use quantitative dose-response modelling for the derivation of the RfD. Other issues include the following:

- Presenting the RfD as a single point value or as a range to reflect the inherent imprecision of the RfD;

- Selecting specific guidance documents for derivation of noncancer health effect levels;

- Considering severity of effect in the development of the RfD;

- Using less-than-90-day studies as the basis for RfDs;

- Integrating reproductive/developmental, immunotoxicity, and neurotoxicity data into the RfD calculation;

- Applying pharmacokinetic data in risk assessments; and

- Considering the possibility that some noncarcinogenic effects do not exhibit a threshold.

(a) Using the Current NOAEL-UF Based RfD Approach or Adopting More Quantitative Approaches for Noncancer Risk Assessment

The current NOAEL-UF-based RfD methodology, or its predecessor ADI/SF methodology, have been used since 1980. This approach assumes that there exists a threshold exposure below which adverse noncancer health effects are not expected to occur. Exposures above this threshold are believed to pose some risk to exposed individuals; however, the current approach does not address the nature and magnitude of the risk above the threshold level (i.e., the shape of the dose-response curve above the threshold). The NOAEL-UF-based RfD approach is intended primarily to ensure that the RfD value derived from the available data falls below the population effects threshold. However, the NOAEL-UF-based RfD procedure has limitations. In particular, this method requires that one of the actual experimental doses used by the researchers in the critical study be selected as the NOAEL or LOAEL value. The determination that a dose is a NOAEL or LOAEL

will depend on the biological endpoints used and the statistical significance of the data. Statistical significance will depend on the number and spacing of dose groups and the numbers of animals used in each dose group. Studies using a small number of animals can limit the ability to distinguish statistically significant differences between measurable responses seen in dose groups and control groups. Furthermore, the determination of the NOAEL or LOAEL also depends on the dose spacing of the study. Doses are often widely spaced, typically differing by factors of three to ten. A study can identify a NOAEL and a LOAEL from among the doses studied, but the "true" NOAEL cannot be determined from those results. The study size and dose spacing limitations also limit the ability to characterize the nature of the expected response to exposures between the observed NOAEL and the LOAEL values.

The limitations of the NOAEL-UF approach have prompted development of alternative approaches that incorporate more quantitative dose-response information. The traditional NOAEL approach for noncancer risk assessment has often been a source of controversy and has been criticized in several ways. For example, experiments involving fewer animals tend to produce higher NOAELs and, as a consequence, may produce higher RfDs. The reverse would seem more appropriate in a regulatory context because larger sample sizes should provide greater experimental sensitivity. The focus of the NOAEL approach is only on the dose that is the NOAEL, and the NOAEL must be one of the experimental doses. It also ignores the shape of the dose-response curve. Thus, the slope of the dose-response plays little role in determining acceptable exposures for human beings. Therefore, in addition to the NOAEL-UF-based RfD approach described above, EPA is considering using other approaches that incorporate more quantitative dose-response information in appropriate situations for the evaluation of noncancer effects and the derivation of RfDs.

However, the Agency wishes to emphasize that it still believes the NOAEL-UF RfD methodology is valid and can continue to be used to develop RfDs.

Two alternative approaches that may have relevance in assisting in the derivation of the RfD for a chemical are the BMD and the Categorical Regression approaches. These alternative approaches may overcome some of the inherent limitations in the NOAEL-UF approach. For example, the BMD analyses for developmental effects show that NOAELs from studies correlate well with a 5 percent response level (Allen et al., 1994). The BMD and the Categorical Regression approaches usually have greater data requirements than the RfD approach. Thus, it is unlikely that any one approach will apply to every circumstance; in some cases, different approaches may be needed to accommodate the varying data bases for the range of chemicals for which water quality criteria must be developed. Acceptable approaches will satisfy the following criteria: (1) meet the appropriate risk assessment goal; (2) adequately describe the toxicity data base and its quality; (3) characterize the endpoints properly; (4) provide a measure of the quality of the "fit" of the model when a model is used for dose-response analysis; and (5) describe the key assumptions and uncertainties.

(1) The Benchmark Dose

The BMD is defined as the statistical lower confidence limit on the dose estimated to produce a predetermined level of change in response (the Benchmark Response, or BMR) relative to control. In the derivation of an RfD, the BMD is used as the dose to which uncertainty factors are applied instead of the NOAEL. The BMD approach first models a dose-response curve for the critical

effect(s) using available experimental data. Several functional forms can be used to model the dose-response curve, such as polynomial or Weibull functions. To define a BMD from the modeled curve for quantal data, the assessor first selects the BMR. The choice of the BMR is critical. For quantal endpoints, a particular level of response is chosen (e.g., 1 percent, 5 percent, or 10 percent). For continuous endpoints, the BMR is the degree of change from controls and is based on what is considered a biologically significant change. The BMD is derived from the BMR dose by applying the desired confidence limit calculation. The RfD is obtained by dividing the BMD by one or more uncertainty factors, similar to the NOAEL approach. Because the BMD is used like the NOAEL to obtain the RfD, the BMR should be selected at or near the low end of the range of increased risks that can be detected in a study of typical size. Generally, this falls in the range between the ED_{01} and the ED_{10}.

The Agency is considering the use of a BMD approach to derive RfDs for those agents for which there is an adequate data base. There are a number of technical decisions associated with the application of the BMD technique. These include the following:

- Selection of response data to model;
- The form of the data used (continuous versus quantal);
- The definition of an adverse response;

- The choice of mathematical model (including use of nonstandard models for unusual data sets);

- The choice of the measures of increased risk (extra risk versus additional risk);

- The selection of the BMR;

- Methods for calculating the confidence interval;

- Selection of the appropriate BMD as the basis for the RfD (when multiple endpoints are modeled from a single study, when multiple models are applied to a single response, and when multiple BMDs are calculated from different studies); and

- The use of uncertainty factors with the BMD approach.

These topics are discussed in detail in Crump et al. (1995) and the TSD that accompanies this Notice. The use of the BMD approach has been discussed in general terms by several authors (Gaylor, 1983; Crump, 1984; Dourson et al., 1985; Kimmel and Gaylor, 1988; Brown and Erdreich, 1989; Kimmel, 1990). The International Life Sciences Institute (ILSI) also held a major workshop on the BMD in September 1993; the workshop proceedings are summarized in ILSI (1993) and in Barnes et al. (1995). For further information on these technical issues, the reader is referred to these publications.

The BMD approach addresses several of the quantitative or statistical criticisms of the NOAEL approach. These are discussed at greater length in Crump et al. (1995) and are summarized here. First, the BMD approach uses information on variability in the selected study rather than just a single data point, such as the NOAEL or LOAEL. By using response data from all of the dose groups to model a dose-response curve, the BMD approach allows for consideration of the steepness of the slope of the curve when estimating the ED_{10}. The use of the full data set also makes the BMD approach less sensitive to small changes in data than the NOAEL approach, which relies on the statistical comparison of individual dose groups. The BMD approach also allows consistency in the consideration of the level of effect (e.g., a 10 percent response rate) across endpoints.

The BMD approach accounts more appropriately for the size of each dose group than the NOAEL approach. Laboratory tests with fewer animals per dose group tend to yield higher NOAELs, and thus higher RfDs, because statistically significant differences in response rates are harder to detect. Therefore, in the NOAEL approach, dose groups with fewer animals lead to a higher (less conservative) RfD. In contrast, with the BMD approach, smaller dose groups will tend to have the effect of extending the confidence interval around the ED_{10}; therefore, the lower confidence limit on the ED_{10} (the BMD) will be lower. With the BMD approach, greater uncertainty (smaller test groups) leads to a lower (more conservative) RfD.

There are some issues to be resolved before the BMD approach is used routinely. These were identified in a 1996 Peer Consultation Workshop (USEPA, 1996b). Methods for routine use of the BMD are currently under development by EPA. Several RfCs and RfDs based on the BMD approach are included in EPA's IRIS data base. These include that for methyl mercury based on

delayed postnatal development in humans; carbon disulfide based on neurotoxicity; 1,1,1,2-tetrafluoroethane based on testicular effects in rats; and antimony trioxide based on chronic pulmonary interstitial inflammation in female rats.

Various mathematical approaches have been proposed for modeling developmental toxicity data (e.g., Crump, 1984; Kimmel and Gaylor, 1988; Rai and Van Ryzin, 1985; Faustman et al., 1989), which could be used to calculate a BMD. Similar methods can be used to model other types of toxicity data, such as neurotoxicity data (Gaylor and Slikker, 1990, 1992; Glowa and MacPhail, 1995). The choice of the mathematical model may not be critical, as long as estimation is within the observed dose range. Since the model is used only to fit the observed data, the assumptions in a particular model regarding the existence or absence of a threshold for the effect may not be pertinent (USEPA, 1997). Thus, any model that suitably fits the empirical data is likely to provide a reasonable estimate of a BMD. However, research has shown that flexible models that are nonsymmetric (e.g., the Weibull) are superior to symmetric models (e.g., the probit) in estimating the BMD because the data points at the higher doses have less influence on the shape of the curve than at low doses. In addition, models should incorporate fundamental biological factors where such factors are known (e.g., intralitter correlation for developmental toxicity data) in order to account for as much variability in the data as possible. The Agency is currently supporting research studies to evaluate the application of several models to data sets for calculating the BMD.

(2) Categorical Regression

Categorical Regression is an emerging technique that may have relevance for the derivation of RfDs or for estimating risk above the RfD (Dourson et al., 1997; Guth et al., 1997). The Categorical Regression approach, like the BMD approach, can be used to estimate a dose that corresponds to a given probability of adverse effects. This dose would then be divided by uncertainty factors to establish a reference dose. However, unlike the BMD approach, the Categorical Regression approach can incorporate information on different health endpoints in a single dose-response analysis. For those health effects for which studies exist, responses to the substance in question are grouped into severity categories; for example (1) no effect, (2) no adverse effect, (3) mild-to-moderate adverse effect, and (4) frank effect. These categories correspond to the dose categories currently used in setting the RfD, namely, the no-observed-effect level (NOEL), NOAEL, LOAEL, and frank-effect level (FEL), respectively. Logistic transform or other applicable mathematical operations are used to model the probability of experiencing effects in a certain category as a function of dose (Harrell, 1986; Hertzberg, 1989). The "acceptability" of the fit of the model to the data can be judged using several statistical measures, including the χ^2 statistic, correlation coefficients, and the statistical significance of its model parameter estimates.

The resulting function can be used to find a dose (or the lower confidence bound on the dose) at which the probability of experiencing adverse effects does not exceed a selected level, e.g., 10 percent. This dose (like the NOAEL or BMD) would then be divided by relevant uncertainty factors to calculate a RfD. For more detail on how to employ the categorical regression approach, see the discussion in the TSD.

As with the BMD approach, the Categorical Regression approach has the advantage of using more of the available dose-response data to account for response variability as well as accounting for uncertainty due to sample size through the use of confidence intervals. Additional advantages of categorical regression include the combining of data sets prior to modeling, thus allowing the calculation of the slope of a dose-response curve for multiple adverse effects rather than only one effect at a time, and the ability to estimate risks for different levels of severity from exposures above the RfD.

On the other hand, as with BMD, opinions differ over the amount and adequacy of data necessary to implement the method. The Categorical Regression approach also requires judgments regarding combining data sets, judging goodness-of-fit, and assigning severity to a particular effect. Furthermore, this approach is still in the developmental stage. It is not recommended for routine use, but may be used when data are available and justify the extensive analyses required.

(3) Summary

Whether a NOAEL-based methodology, a BMD, a Categorical Regression model, or other approach is used to develop the RfD, the dose-response-evaluation step of a risk assessment process should include additional discussion about the nature of the toxicity data and its applicability to human exposure and toxicity. The discussion should present the range of doses that are effective in producing toxicity for a given agent; the route, timing, and duration of exposure; species specificity of effects; and any pharmacokinetic or other considerations relevant to extrapolation from

the toxicity data to human-health-based AWQC. This information should always accompany the characterization of the adequacy of the data.

(b) Presenting the RfD as a Single Point or as a Range for Deriving AWQC

Although the RfD has traditionally been presented and used as a single point, its definition contains the phrase ". . . an estimate (with uncertainty spanning perhaps an order of magnitude) . . ." (USEPA, 1993a). Underlying this concept is the reasoning that the selection of the critical effect and the total uncertainty factor used in the derivation of the RfD is based on the "best" scientific judgment, and that competent scientists examining the same data base could derive RfDs which varied within an order of magnitude.

In one case, the RfD was presented as a point value within an accompanying range. EPA derived a single number as the RfD for arsenic (0.3 µg/kg-day), but added that "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, 1993c). EPA noted that regulatory managers should be aware of the flexibility afforded them through this action.

In today's Notice, EPA discusses situations where the risk manager can consider a range around the point estimate. As explained further below, the Agency is recommending that sometimes considering the use of a range for the RfD is more appropriate in characterizing risk than only the use of the point estimate. The selection of an appropriate range must be determined for each individual situation, since several factors affect the magnitude of the range associated with the RfD.

For example, the completeness of the data base plays a major role. Observing similar effects in several animal species, including humans, can increase confidence in the selection of the critical effect 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, dose spacing, and possibly the route of the experimental doses. For example, a steep dose-response curve indicates that relatively large differences in response occur with a small change in dose. For chemicals that elicit a serious effect near the LOAEL, an additional uncertainty factor is often used in the RfD derivation to protect against less serious but still observable adverse effects that could occur at lower doses, thus increasing the range of uncertainty for the RfD. Dose spacing and the number of animals in the study groups used in the experiment can also affect the confidence in the RfD.

To derive the AWQC, the point estimate of the RfD is the default. Based on considerations of available data, the use of another number within the range defined by the UF could be justified in a specific case. This means that there are risk considerations 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.

Because the uncertainty around the dose-response relationship increases as extrapolation below the observed data increases, the use of a point within the RfD range may be more appropriate in characterizing the risk than the use of the 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 because there is great confidence in the hazard and dose-response characterization. If greater than 100 and 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. Use of any point other than the RfD must be justified.

The following examples illustrate situations where EPA believes the use of a range is not appropriate. The RfD for zinc (USEPA, 1992) is based on consideration of nutritional data, a minimal LOAEL, and a UF of 3. If a 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. Another case in point is nitrate. Since the RfD for nitrate was based on the lack of effects in human infants and was assigned a UF of 1 (USEPA, 1991b), it would be difficult if not impossible to justify the use of an

TABLE IIIB-2. SOME SCIENTIFIC FACTORS TO CONSIDER WHEN USING THE RFD RANGE

Use point estimate RfD	- Default position - Total uncertainty factor, modifying factor product 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 large uncertainty factor - A steep dose-response curve in the range of observation - No sensitive populations identified

RfD range for infants exposed to nitrate. Table IIIB-2 gives examples of factors to consider when determining whether to use the point estimate of the RfD, or a value higher or lower than the point estimate (see the TSD for additional detail on this topic).

The risk-characterization step of the risk assessment provides a mechanism for communicating such issues. The risk manager must be informed of those specific cases when it is not scientifically correct to estimate a RfD range. In addition, the risk characterization should provide risk managers with guidelines (see Table IIIB-2) on the scientific basis for using a value within the range as the RfD.

(c) Guidelines to be Adopted for Derivation of Noncancer Health Effects Values

The Agency is currently using IRIS Background Document 1A entitled *Reference Dose (RfD): Description and Use in Health Risk Assessments* as the general basis for the risk assessment of noncarcinogenic effects of chemicals (USEPA, 1993a). EPA recommends continued use of this document for this purpose. However, it should be noted that the process for evaluating chemicals for inclusion in IRIS is undergoing revision. The Agency is currently conducting a pilot program for the continued development of the IRIS assessment process. Under this program, a more integrated assessment for cancer and noncancer effects is being developed for 11 chemicals: arsenic, bentazon, beryllium, chlordane, chromium compounds, cumene, methyl methacrylate, methylene diphenyl isocyanate, napthalene, tributyltin oxide and vinyl chloride (USEPA, 1996c). The results for these 11 are expected to be in IRIS soon. A second set of chemical assessments have also been initiated and are expected to be complete by the end of 1998. The second set includes the following

eight chemicals: acetonitrile; barium; benzene; 1,3-butadiene; cadmium; chloroethane; diesel emissions; and ethylene glycol butyl ether (USEPA 1998). A third set of chemicals is planned for completion by the end of 1999, which includes boron; bromate; chloral hydrate; chloroform; dichloroacetic acid; 1,3-dichloropropene; formaldehyde; lindane; nitrobenzene; pentachlorophenol; PCBs (noncancer endpoints); styrene; tetrachloroethylene; tetrahydrofuran; toxaphene; trichloroethylene; and vinyl acetate (USEPA, 1998).

(d) Treatment of Uncertainty Factors/Severity of Effects During the RfD Derivation and Verification Process

During the RfD derivation and review process, EPA considers the uncertainty of extrapolations between animal species and within individuals of a species, as well as specific uncertainties associated with the completeness of the data base, as described in Table IIIB-1.

The Agency's RfD Work Group has always considered the severity of the observed effects induced by the chemical under review when choosing the value of the UF with a LOAEL. For example, during the derivation and verification of the RfD for zinc (USEPA, 1992), an uncertainty factor less than the standard factor of 10 (UF of 3) was assigned to the relatively mild adverse effects seen in experimental studies in humans, namely, a decrease in erythrocyte superoxide dismutase activity. EPA recommends that an assessment of the severity of the critical effect be determined when deriving an RfD and that risk managers be made aware of the severity of the effect and the weight placed on this attribute of the effect when the RfD was derived.

(e) Use of Less-Than-90-Day Studies to Derive RfDs

Generally, less-than-90-day experimental studies are not used to derive an RfD. This is based on the rationale that studies lasting for less than 90 days may be too short to detect various toxic effects. However, EPA, has in certain circumstances, derived an RfD based on a less-than-90-day study. For example, the RfD for nonradioactive effects of uranium is based on a 30-day rabbit study (USEPA, 1989). The short-term exposure period was used since it was adequate for determining doses that cause chronic toxicity. In other cases, it may be appropriate to use a less-than-90-day study because the critical effect is expressed in less than 90 days. For example, the RfD for nitrate was derived and verified using studies that were less than 3-months duration (USEPA, 1991b). The reason for this decision was that the critical effect, methemoglobinemia in infants, occurs in less than 90 days. When it can be demonstrated from other data in the toxicological data base that the critical adverse effect is expressed within the study period and that a longer exposure duration would not exacerbate the observed effect or cause the appearance of some other adverse effect, the Agency may choose to use less-than-90-day studies as the basis of the RfD. Such values would have to be used with care because of the uncertainty in determining if other effects might be expressed if exposure was of greater duration than 90 days.

(f) Use of Reproductive/Developmental, Immunotoxicity, and Neurotoxicity Data as the Basis for Deriving RfDs

All relevant toxicity data have some bearing on the RfD derivation and verification and are considered by EPA. The "critical" effect is the adverse effect most relevant to humans or, in the

absence of an effect known to be relevant to humans, the adverse effect that occurs at the lowest dose in animal studies. For example, if the critical effect is neurotoxicity, EPA may use this specific toxicity data as the basis for the derivation and verification of an RfD, as it did for the RfD for acrylamide. Moreover, the Agency is continually revising its procedures for noncancer risk assessment. For example, EPA has recently released guidelines for deriving developmental RfDs (RfD_{DT}, USEPA, 1991a), for using reproductive toxicity (USEPA, 1996a), and neurotoxicity (USEPA, 1995) data in risk assessments. The Agency is currently working on guidelines for using immunotoxicity to derive RfDs. In addition, the Agency is proceeding with the process of generating acceptable emergency health levels for hazardous substances in acute exposure situations based on established guidelines (NRC, 1993).

(g) Applicability of Physiologically Based Pharmacokinetic (PBPK) Data in Risk Assessment

EPA believes that all pertinent data should be used in the risk assessment process, including PBPK data. In fact, the Agency has used PBPK data in deriving the RfD for cadmium and other compounds. In addition, the Agency is currently using PBPK data to better characterize human inhalation exposures from animal inhalation experiments during derivation/verification of RfCs. In analogy to the RfD, the RfC is considered to be an estimate of a level in the air that is not anticipated to cause adverse effects over a lifetime of inhalation exposure (Jarabek et al., 1990). With RfCs, a kinetic adjustment is made for the differences between animals and humans in respiration and deposition. This procedure results in calculation of a "human equivalent concentration." Based on

the use of these procedures, an interspecies UF of 3 (i.e., approximately $10^{0.5}$), instead of the standard factor of 10, is used in the RfC derivation.

The rationale for the use of PBPK models is that the pharmacokinetics and pharmacodynamics of a chemical each contribute to a chemical's observed toxicity, and specifically, to observed differences among species in sensitivity. Pharmacokinetics describes the absorption, distribution, metabolism, and elimination of chemicals in the body, while pharmacodynamics describes the toxic interaction of the agent with the target cell. In the absence of specific data on their relative contributions to the toxic effects observed in species, each is considered to account for approximately one-half of the variability in observed effects, as is assumed in the development of RfCs and RfDs. The implication of this assumption is that an interspecies uncertainty factor of 3 rather than 10 could be used for deriving an RfD when valid pharmacokinetic data and models can be applied to obtain an oral "human equivalent applied dose" (Jarabek et al., 1990). If specific data exist on the relative contribution of either element to observed effects, that proportion will be used.

(h) Consideration of Linearity (or Lack of a Threshold) for Noncarcinogenic Chemicals

It is quite possible that there are chemicals with noncarcinogenic endpoints that have no threshold exposure level. For example, it appears that, after skin sensitization occurs from exposure to nickel, there is no apparent threshold in subpopulations of hypersensitive individuals for subsequent dermal effects of the chemical. Other examples could include genotoxic teratogens and germline mutagens. Genotoxic teratogens act by causing mutational events during organogenesis,

histogenesis, or other stages of development. Germline mutagens interact with germ cells to produce mutations which may be transmitted to the zygote and expressed during one or more stages of development. However, there are few chemicals which currently have sufficient mechanistic information about these possible modes of action. It should be recognized that although a mode of action consistent with linearity is possible (especially for agents known to be mutagenic), this has yet to be reasonably demonstrated for most toxic endpoints other than cancer.

EPA has recognized the potential for nonthreshold noncarcinogenic endpoints and discussed this issue in the *Guidelines for Developmental Toxicity Risk Assessment* (USEPA, 1991a) and in the 1986 *Guidelines for Mutagenicity Risk Assessment* (USEPA, 1986). An awareness of the potential for such teratogenic/mutagenic effects should be established in order to deal with such data. However, without adequate data to support a genetic or mutational basis for developmental or reproductive effects, the default becomes an uncertainty factor or mechanism of action approach, which are procedures utilized for noncarcinogens assumed to have a threshold. Therefore, genotoxic teratogens and germline mutagens should be considered an exception while the traditional uncertainty factor approach is the general rule for calculating criteria or values for chemicals demonstrating developmental/ reproductive effects. For the exceptional cases, 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. Other types of nonthreshold noncarcinogens must also be handled on a case-by-case basis.

(i) Minimum Data Requirements

For details on minimum data requirements related to RfD development, see the TSD.

4. SAB Comments

The SAB commented that the BMD approach, and other approaches, have strengths and weaknesses. As described previously, these approaches permit use of more of the entire data base, derive a number that is independent of dose spacing, and can be applied in a manner that reflects the quality of the data. The SAB counseled against using a low BMD (e.g., ED_{01}) that is outside the dose range able to be detected by current toxicological methodology. The SAB further mentioned that the "threshold" for a noncancer effect must be considered when using these approaches. EPA does not disagree with the SAB comments on the BMD and other new approaches for dose-response evaluation. The AWQC Methodology allows for using the benchmark, categorical regression or traditional approach (i.e., NOAEL/LOAEL) in deriving an RfD. This allows for flexibility in choosing the approach that best suits the data. In most cases, the concept of a threshold will be intrinsic to the risk characterization for noncarcinogens. However, as pointed out in Section B.3(h), there are some toxins (such as lead) that appear to have no threshold.

The SAB has expressed the opinion that few data demonstrate that the precision of the RfD derivation process is "an order of magnitude" and mentioned that the precision of each RfD is specific for that RfD. The SAB also questions the application of the term "precision" in this case, because of the difficulty in evaluating the precision of a particular RfD. In responding to comments, EPA attempted to remove terminology that implied that there was an order of magnitude in the precision of the RfD but still allowed for choosing a value other than the point estimate of the RfD

in establishing the AWQC. The acceptable range around the RfD has been tied to the uncertainty in the data, rather than any assessment of the analytical precision or accuracy of the calculation. The word precision is still used in the text, but, hopefully, in a context that implies a general rather than analytical meaning.

The SAB concurs that the severity of effect should be considered during the RfD derivation and verification process. However, the SAB has expressed concern about the type of scale that would be used to rate the level of severity. SAB suggests that a severity scale could be based on whether the effect is reversible or if it is irreversible and cumulative. Another possible construct could consider whether the effect is an overt pathology, functional deficit, adverse biochemical change, or a biochemical change of unknown consequence. Finally, a severity scale could be developed based on consideration of target organ affected. The SAB commented that the second type of scale is likely to have greatest applicability to noncancer effects, and would require that biochemical effects be specifically related to functional changes and/or to overt pathology. The SAB expressed skepticism about scales based on relative value given to target organ systems. EPA agrees that it is difficult to develop a simple scale for expressing the severity of an effect. Such a judgment is best left to experienced toxicologists. References for guidelines to consider in evaluating the seriousness of effects are included in the TSD as resource information for the reader.

The SAB has expressed the opinion that, as a rule, less-than-90-day studies are not adequate for RfD derivation, and cited the danger of false-negative studies. It believes that RfDs derived in this manner should be labeled as "temporary" or "interim." However, as demonstrated above, each case must be considered individually. The AWQC guidelines are in agreement with SAB regarding

the use of data from studies of less than 90-day duration, but point out that there are circumstances (such as occurrence of a critical acute effect or a developmental RfD) where data from durations of less than 90-days are used.

The SAB believes that PBPK modeling is useful for RfD derivation but needs to be based on understanding the mechanisms of toxicity. EPA is in general agreement with the SAB's opinions about the limitations on the use of PBPK data, and require that pharmacokinetic models be verified and understood before they are used. This implies that there is an understanding of the pharmacodynamic interactions of the toxic agent with a target cell.

5. Request for Comments

1. EPA requests comment on the application of the NOAEL-UF, BMD, Categorical Regression, and other approaches to derive RfDs in support of the derivation of AWQC for the protection of human health.

2. EPA requests comment on the issue of permitting the use of a point within the RfD range for deriving the AWQC, rather than a single point estimate. It must be emphasized that appropriate scientific justification must be given when using any number other than the point estimate RfD. EPA requests comment on how to develop the RfD range and how to determine which point estimate in the range is appropriate.

3. EPA requests comment on approaches to incorporate severity of effect in deriving the RfD.

4. EPA requests comment on the use of less-than-90-day studies to derive RfDs.

5. EPA requests comment on the use of reproductive/developmental, immunotoxicity, and neurotoxicity data as the basis for deriving RfDs.

6. EPA requests comment on the use of PBPK data in deriving an RfD.

7. EPA requests comment on allowing, on a case-by-case basis, consideration of a nonthreshold mode of action for certain chemicals that cause noncancer effects when deriving RfDs.

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C. Exposure

As discussed in the Introduction, the derivation of AWQC for the protection of human health requires information about both the toxicological endpoints of concern for water pollutants and the pathways of human exposure to those pollutants. Historically, two primary pathways of human exposure to pollutants present in a particular ambient waterbody have been considered in deriving AWQC: direct ingestion and other exposure from household uses (e.g., showering) of drinking water obtained from that waterbody, and the consumption of fish/shellfish indigenous to that waterbody. A third pathway that has also been of concern in some circumstances is incidental ingestion of ambient water in conjunction with recreational uses. The derivation of an ambient water quality criterion for a pollutant entails the calculation of the maximum water concentration of that pollutant which ensures that drinking water exposures and/or fish consumption, as well as incidental ingestion,

do not result in human intake of that pollutant in amounts that exceed a specified level based upon the toxicological endpoint of concern.

There are many exposure topics and issues involved in the derivation of AWQC. The first category includes several broad policy issues concerning the major objectives that the Agency believes should be met in setting AWQC. These issues include the following:

- Specifying which sources of exposure associated with ambient water should be explicitly included in the derivation of AWQC (e.g., Should drinking water be included in AWQC given that there may be separate national drinking water standards? Should AWQC be separate for drinking water exposure and fish consumption, or should they reflect combined exposure potential? Should there be an AWQC based on incidental water ingestion?)

- Identifying which segment or subgroup of the population AWQC should be designed to protect (e.g., Should the derivation be based on providing protection for individuals having average or "typical" exposures? Should it be based on protecting highly exposed individuals, or most sensitive individuals?)

The second category includes determining whether nonwater sources of exposure (e.g., dietary, inhalation) should also be explicitly considered in the derivation of AWQC. (i.e., Should they be included when setting AWQC based on carcinogenicity as the toxicological endpoint?

Should they be considered when setting AWQC based on an RfD for a noncarcinogenic endpoint? What specific procedures should be followed to account for the nonwater sources?)

The third category of issues involves those that mainly address the selection of specific values for the exposure factors included in the AWQC derivation algorithms and which (for the most part) involve considerations independent of the particular method or procedure selected for deriving the criterion. These include such considerations as drinking water consumption rates, fish ingestion rates, and human body weight.

The following sections present exposure issues relevant to the Draft AWQC Methodology Revisions, organized according to the three topics introduced above: policy issues are presented first, followed by the consideration of nonwater sources of exposure, and finally the factors used in AWQC computation. In relevant sections, comments provided from the SAB in its August 1993 review of the AWQC methodology are presented and discussed.

The TSD presents suggested sources of contaminant concentration and exposure intake information, in addition to some suggestions of survey methods for obtaining and analyzing exposure data, necessary for setting AWQC. The following topics are also addressed in the TSD accompanying this Notice regarding exposure assessments for the AWQC: evaluating available exposure data; describing highly exposed subpopulations; distinguishing between major and minor exposure sources; comparing exposures to RfD values; addressing uncertainty and variability of the estimate; the question of current and future uses of the chemical; considering chemical and physical properties; and addressing unquantifiable exposures via an allocation ceiling.

1. Policy Issues

The following discussions are qualitative in nature and are discussed in greater detail in Section C.3., Factors Used in the AWQC Computation.

(a) Identifying the Population Subgroup that the AWQC Should Protect

The AWQC criteria are derived to establish ambient concentrations of chemicals which, if not exceeded, will protect the general population from adverse health impacts from that chemical due to consumption of aquatic organisms and water, including incidental water consumption related to recreational activities. For each chemical, chronic criteria are derived to reflect long-term consumption of food and water. An important decision to make when setting AWQC is the choice of the particular population to protect. For instance, the criteria might be set to protect those individuals who have average or "typical" exposures, or the criteria could be set so that they offer greater protection to those individuals who are more highly exposed (e.g., subsistence fishers). EPA has selected default assumptions that are representative of the defined populations being addressed. These defined populations are: adults in the general population; sport (recreational) fishers; subsistence fishers; women of childbearing age (defined as ages 15-44); and children. In deciding on default assumptions, EPA is aware that multiple assumptions are used in combination (e.g., intake rate and body weight). In the section on the exposure factors used in the AWQC computations, EPA describes the populations that are represented by the different exposure intake assumptions. EPA recommends that priority should be given to identifying and adequately protecting the most highly exposed population. In carrying out regulatory actions under its statutory authorities, including the

CWA, EPA's risk management goal is to establish criteria that are protective of human health and generally views that an upper-bound incremental cancer risk in the range of 10^{-5} to 10^{-6} achieves this goal. EPA also considers that the goal is satisfied if the population as a whole will be adequately protected by human health criteria when the criteria are met in ambient water. As stated previously in Appendix II, Section A, EPA is proposing criteria at the 10^{-6} risk level. However, States and Tribes should have the flexibility to develop criteria, on a site-specific basis, that provides additional protection appropriate for highly exposed populations. EPA understands that highly exposed populations may be widely distributed geographically throughout a given State and Tribal area. Thus, if the State or Tribe determines that a highly exposed population would not be adequately protected by criteria based on the general population, EPA recommends that the State/Tribe adopt more stringent criteria. Furthermore, EPA recommends that States and Tribes ensure that the most highly exposed populations not exceed a risk level of 10^{-4}. EPA acknowledges that at any given risk level for the general population, those segments of the population that are more highly exposed face a higher relative risk. For example, if fish are contaminated at a level permitted by criteria that are derived based on a risk level of 10^{-6}, individuals consuming up to 10 times the assumed fish consumption rate would still be protected at a 10^{-5} risk level.

For RfD-based chemicals, EPA's policy is that, in general, the RfD should not be exceeded (see discussion in Section B.3.b on the RfD range) and that the exposure assumptions used should reflect the population of concern. It is recommended that when setting waterbody-specific AWQC, States and Tribes should consider the populations most exposed via water and fish.

(b) Appropriateness of Including the Drinking Water Pathway in AWQC

Under the 1980 AWQC National Guidelines, the derivation of AWQC for the protection of human health accounted for potential human exposure via both consumption of drinking water and ingestion of fish. During the 1992 Workshop, there was discussion regarding the need to include drinking water consumption as a factor in calculating AWQC for surface waters. The principal argument presented against the explicit inclusion of drinking water consumption is that most drinking water, and almost all drinking water obtained from surface water sources, is treated prior to its distribution to consumers. That is, the direct ingestion of untreated ambient water is extremely rare and, therefore, direct ingestion of water should only be taken into account in setting AWQC when it is a significant route of exposure for a population of concern. However, the majority opinion from the 1992 workshop was that direct ingestion is relevant to the AWQC (for the reasons stated below).

EPA recommends continuing to include the drinking water exposure pathway explicitly in deriving AWQC for the protection of human health where drinking water is a designated use, for the following reasons: (1) drinking water is a designated use for surface waters under the CWA and, therefore, criteria are needed to assure that this designated use can be maintained; (2) although rare, there are some public water supplies that provide drinking water from surface water sources without treatment; (3) even among the majority of water supplies that do treat surface waters, existing treatments may not necessarily be effective for reducing levels of particular contaminants; (4) in consideration of the Agency's goals of pollution prevention, ambient waters should not be contaminated to a level where the burden of achieving health objectives is shifted away from those

responsible for pollutant discharges and placed on downstream users to bear the costs of upgraded or supplemental water treatment.

(c) Relationship Between Human Health AWQC and Drinking Water Standards

In conjunction with the preceding issue, EPA has also given consideration to whether there should be an equivalency between the drinking water component of AWQC and either MCLGs or MCLs promulgated under the SDWA.

Under the SDWA, MCLGs are established as health-based goals without explicit consideration of either the costs or technological feasibility of achieving those goals. MCLs are then set as close to the MCLGs as possible, taking costs of the drinking water treatment technologies and the availability of analytical methodologies into account. Because MCLs are based in part on cost and technology considerations, they are not considered counterparts to AWQC for the protection of human health. As strictly health-based goals, however, MCLGs and AWQC for the protection of human health are highly analogous. There are some states that have utilized MCLGs as human health water quality criteria under the CWA.

The application of the health goals set under the SDWA is quite different from the application of goals set under the CWA. Under the SDWA, the MCLGs (and MCLs) apply to the chemical concentration in distributed tap water, whereas under the CWA, AWQC are used to develop State or Tribal standards, which are then used with water transport models to derive permit limits for point source discharges. Because the water transport model uses protective assumptions

which provide a margin of safety (such as 30-year, low-flow rates), it is generally unlikely that the water column concentration will be as high as the AWQC concentration limit for an extended period of time.

In some cases, MCLs or MCLGs are more stringent than AWQC. In other cases, AWQC are more stringent than the drinking water MCLs or MCLGs. The reason is that the methodology used for deriving drinking water levels is different than the methodology used for deriving AWQC. Although both methods predominantly use the same reference dose or cancer risk assessment, and both methods assume a 70 kg adult and consumption of 2 liters of water per day, there are several important risk management differences. One difference is that MCLGs for chemicals that are known or likely carcinogens have usually been set equal to zero, while AWQC for carcinogens are based on an incremental cancer risk level. For chemicals with limited evidence of carcinogenicity (classified as C, possible carcinogen, under the 1986 Cancer Guidelines), the MCLG is usually based on the chemical's reference dose for noncancer effects with the application of an additional uncertainty factor of 1 to 10 to account for its possible carcinogenicity. The 1980 AWQC guidelines do not differentiate among carcinogens with respect to the weight-of-evidence grouping; all were derived based on lifetime carcinogenic risk levels. Another difference is that a single determined risk value (i.e., within the range of 10^{-4} to 10^{-6}) is selected in setting risk-based MCLs, while AWQC have been derived by providing incremental risk levels spanning 10^{-5} to 10^{-7} (i.e., three values were presented). Different numerical values between the two may also be due to the information that each criterion is based on at the time of development. That is, criteria developed at different times for the same chemical may be based on different exposure data and, perhaps, different toxicity studies. However, the principal difference is in the approach to accounting for exposure sources, including

the fact that AWQC are based on a prediction of exposure from fish and shellfish using a bioaccumulation factor for the individual chemical and a fish/shellfish consumption rate. With the current MCLG methodology, bioaccumulation factors have not been used in the exposure estimates and fish/shellfish consumption rates have not been fully accounted for. Additionally, MCLGs for RfD-based chemicals developed under the SDWA follow a relative source contribution (RSC) approach in which the percentage of exposure that is attributed to drinking water is determined relative to the total exposure from all sources (e.g., drinking water, food, air). The rationale for this approach is to ensure that an individual's total exposure to a chemical does not exceed the RfD. Although the 1980 AWQC guidelines recommended taking non-fish dietary sources and inhalation into account, data on these other sources were generally not available. Therefore, it was typically assumed that an individual's total exposure to a chemical came solely from drinking water from the water body and consumption of fish and shellfish living in the water body. Lastly, as stated previously, when an MCL is adjusted based on cost or availability of treatment technology or analytical methods, then the MCL may become much less stringent than the AWQC, regardless of the exposure assumptions or toxicological basis.

The SAB, in its 1993 review of EPA's preliminary recommendations, commented that there would be difficulties in using the concept of drinking water MCLGs for setting AWQC. The SAB was concerned about the possible introduction of the zero MCLG concept into the methodology for deriving AWQC. The SAB was also concerned that AWQC are considerably different from MCLGs, and that developing AWQC that are different from MCLGs may be reasonable in certain specific cases (e.g., for disinfectant byproducts). EPA's proposed methodology addresses the specific concerns that the SAB has raised regarding the incorporation of the zero MCLG concept.

The Agency believes that for a given pollutant, the drinking water component of an AWQC should be consistent with the MCLG that has been established for that substance (if one has been developed) and, therefore, proposes to use similar assessment methodologies for deriving AWQC and MCLGs. EPA stated its policy on the use of Section 304(a) human health criteria (i.e., the AWQC) versus MCLs in 45 FR 79318, November 28, 1980. Additionally, a memorandum from R. Hanmer to the Regional Water Management Division Directors dated December 12, 1988, provided detailed guidance with regard to this policy. Specifically, for the protection of public water supplies, EPA encouraged the use of MCLs. When fish ingestion is considered an important activity, EPA recommended the use of AWQC to protect human health. In all cases, if an AWQC did not exist for a chemical, an MCL was deemed a suitable level of protection. EPA is now recommending a slightly different approach. Although the use of MCLs is acceptable in the absence of 304(a) criteria, EPA is recommending that MCLs only be used when they are numerically the same as the MCLG and only when the sole concern is the protection of public water supply sources and not the protection of the CWA section 101(a) goal regarding fish consumption (e.g., where the chemically toxic form in water is not the form found in fish tissue and, therefore, fish ingestion exposure is not an issue of concern). Where consideration of available treatment technology, costs, or availability of analytical methodologies has resulted in MCLs that are less protective than MCLGs or AWQC, States and Tribes should consider using MCLGs and/or health-based AWQC to protect water uses. Where fish consumption is an existing or potential activity, States and Tribes should ensure that their adopted human health criteria adequately address this exposure route. When fish consumption is a use, EPA recommends development of AWQC due to the fact that fish consumption and bioaccumulation are explicitly addressed. In all cases, AWQC should be set to ensure that all routes of exposure have been considered. EPA believes if water monitored at existing drinking water

intakes has concentrations at or below MCLGs, then the water could be considered to meet a designated use under the CWA as a drinking water supply. In situations where a 304(a) criterion was less protective than an MCL, it is advisable to use the MCL as the criterion for segments designated as drinking water supplies. For carcinogens where the MCLG is equal to zero, States are encouraged to base an AWQC at the drinking water intake on an acceptable cancer risk level (i.e., a level within the range of 10^{-4} to 10^{-6}), to promote pollution prevention and anti-degradation.

(d) Setting Separate AWQC for Drinking Water and Fish Consumption

In conjunction with the issue of the appropriateness of including the drinking water pathway explicitly in the derivation of AWQC for the protection of human health, there has been discussion of whether these AWQC should be single values that account for potential exposure from drinking water and fish consumption together, or whether it is more appropriate to calculate separate AWQC explicitly for each pathway. One of the factors considered has been that setting separate criteria could provide a more straightforward means of developing AWQC for the drinking water pathway that would be consistent with MCLG development.

The 1980 AWQC National Guidelines used the approach of setting a single AWQC accounting for both drinking water and fish consumption, as well as a separate AWQC based on ingestion of aquatic organisms alone. This latter criterion was intended to apply in those cases where the designated uses of a waterbody include supporting fish or shellfish for human consumption, but not as a drinking water supply source (e.g., non-potable estuarine waters).

Although the SAB recommended the use of separate criteria based on fish intake and water consumption, in the revised methodology, the Agency is recommending continuing the practice of setting AWQC that account for combined drinking water and fish consumption, as well as a separate criterion for fish/shellfish consumption alone. The reason for this is because most State and Tribal programs designate their waters to cover both uses.

(e) Incidental Ingestion from Ambient Surface Waters

The 1980 AWQC National Guidelines did not include criteria to address incidental ingestion from recreational uses. As noted previously, there are cases where AWQC for the protection of human health do not include consideration of the waterbody as a source of potable water (e.g., estuaries). In these cases, criteria based only on fish ingestion (or aquatic life criteria) may not adequately protect recreational users from health effects resulting from incidental ingestion. In order to protect recreational users, EPA recommends including exposure resulting from incidental ingestion of water in those cases where the waterbody is not used for potable water. However, it should be noted that the SAB felt there was not a great need for incidental ingestion criteria for recreational uses where drinking water criteria are inapplicable (e.g., estuaries). The exposure factors section of this Notice [Appendix II, Section C.3.(c)] discusses incidental ingestion estimates for calculating both chronic and acute ingestion rates.

2. Consideration of Nonwater Sources of Exposure When Setting AWQC

(a) Background

In the 1980 AWQC National Guidelines, different approaches for addressing nonwater 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 fish ingestion) were considered in the derivation of the AWQC. Nonwater sources were not considered explicitly. 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, nonwater exposures were to be considered when deriving the AWQC under the 1980 AWQC National Guidelines. In effect, the 1980 AWQC National Guidelines specified that the AWQC be calculated to account for no more than that portion of the ADI that remains after contributions from other expected sources of exposure have been subtracted out. The ADI is equivalent to the RfD, which is discussed in Appendix II, Section B of this Notice. 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 AWQC National Guidelines recommended taking non-fish dietary sources and inhalation into account in setting the AWQC for threshold contaminants, in practice the data on these other sources were generally not available and, therefore, the AWQC usually were derived such that they accounted for all of the ADI (RfD). When the 1980 AWQC National Guidelines were published, EPA noted that the inability to estimate intake from non-fish dietary sources and inhalation, as well as the wide variability that may exist in such exposures, would add to the uncertainty in the criteria derivation. EPA also noted in the 1980 AWQC National Guidelines that in terms of scientific validity, the accurate estimate of the ADI (RfD) is the major factor in the satisfactory derivation of AWQC.

Note: In the drinking water MCLG methodology, noncarcinogenic criteria follow an RSC approach in which the percentage of exposure that is attributed to drinking water is determined relative to the total exposure from all sources (e.g., drinking water, food, air, soil). The rationale for this approach is to ensure that an individual's total exposure to a chemical does not exceed the reference dose.

Given the inability to reasonably predict future changes in exposure patterns, the uncertainties in the exposure estimates due to both data inadequacy and possible unknown sources of exposure, as well as the potential for some populations to experience greater exposures than indicated by the available data, EPA believes that utilizing the entire RfD (or Pdp/SF) may not be adequately protective. Additionally, the uncertainties associated with the derivation of the RfD (or Pdp/SF) (e.g., limitations in the toxicity study, extrapolation from the study species to humans) are independent of the exposure assessment and the associated intake sources and intake uncertainties.

If the AWQC are set so that the RfD or Pdp/SF (or some ceiling value less than either of these) is not exceeded after taking other sources of exposure into account, a procedure to consider the nonwater sources in the derivation of AWQC must be adopted.

As discussed above, the 1980 AWQC National Guidelines did not account for nonwater sources when setting AWQC for those chemicals that were evaluated as carcinogens. The formula for setting the criterion for carcinogens was:

$$C = \frac{[70 \cdot LR]}{[q_1^* \cdot (2 + 0.0065R)]} \qquad \text{(Equation IIIC-1)}$$

where:

C = The AWQC (mg/L)

70 = human body weight (kg)

LR = lifetime cancer risk factor being used to set the criterion, generally in the range of 10^{-5} to 10^{-7}

q_1^* = cancer slope factor in $(mg/kg\text{-}day)^{-1}$

2 = drinking water consumption (L/day)

0.0065 = fish ingestion (kg/day)

R = bioconcentration factor (L/kg)

As indicated by the above equation, if the lifetime risk value (LR) in the above equation is 10^{-6}, then the value computed for C is the water concentration that would be expected to **increase** an individual's lifetime risk of carcinogenicity from exposure to the particular pollutant by no more than

one chance in one million, regardless of the additional lifetime cancer risk due to exposure, if any, to that particular substance from other sources.

For noncarcinogens for which nonwater exposures were to be considered, however, the 1980 methodology included the following general formula for setting the criterion:

$$C = \frac{[ADI - (DT + IN)]}{[2 + 0.0065R]} \qquad \text{(Equation IIIC-2)}$$

where:

C = The criterion (mg/L)

ADI = Acceptable daily intake (mg), developed as a dose specifically for a 70 kg adult [replaced by the use of Reference Dose (RfD) in units of mg/kg-day, as discussed in Appendix II, Section B of this Notice]

DT = Non-fish dietary intake (mg/kg-day)

IN = Inhalation intake (mg/kg-day)

The other elements are the same as for the cancer-based formula, above. As indicated by the above equation, the 1980 AWQC National Guidelines used a "subtraction" approach to account for nonwater 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 nonwater sources. A similar subtraction approach was used, albeit inconsistently, in the derivation of drinking water MCLG values in the early and mid-1980's; along with a percentage method. More recently, the approach used in the drinking water program has been

to determine the MCLGs exclusively by the percentage method. To foster meeting the objective noted earlier of establishing consistency in deriving MCLGs and the drinking water component of AWQC, EPA would like to use the same approach for both MCLGs and AWQC.

There has been some discussion of whether it is, in fact, necessary in most cases to explicitly account for other sources of exposure when computing the AWQC for pollutants exhibiting threshold effects. It has been argued that because of the conservative assumptions generally incorporated in the calculation of reference doses used as the basis for the AWQC derivation, total exposures slightly exceeding the RfD are unlikely to produce adverse effects. It could be argued, therefore, that reducing AWQC by accounting for other exposure sources relative to what they would be if they were derived from the full RfD value provides little or no actual additional risk reduction.

In its report, SAB's Drinking Water Committee did not feel that it is appropriate to develop AWQC geared to ensure that the sum of all theoretically possible exposures never exceeds the RfD by even a small amount. The Committee rejected the routine use of the percentage or subtraction methods for the allocation of the RfD, and the use of default values in the absence of reliable exposure data. They also expressed concern that EPA could "focus intense regulatory attention on insignificant problems, thus wasting scarce resources" if "compensat[ion] for other routes of exposure" was attempted. (For the complete discussion, refer to SAB, 1993.)

Instead, the Committee endorsed the recommendation from the AWQC Workshop held by the Agency in 1992 which calls for bringing together knowledgeable individuals from all the appropriate offices or agencies for discussions when significant contributions to exposure are

expected from multiple sources, and the total of those contributions exceeds the RfD. For certain chemicals (e.g., dioxin, mercury), EPA has coordinated efforts throughout the Agency. However, such extensively coordinated efforts may prove to be impractical on a routine basis. It is reasonable that the initially developed assessments and proposed criteria, including proposals for RfD allocation, could be circulated for comments and input from staff of the appropriate offices or agencies.

However, the SAB also stated that apportionment can be attempted when data are available. When total exposures are below the RfD, SAB suggested that EPA's goal should be to develop criteria "to ensure that a problem does not develop in the future." Yet, they made no specific suggestions on how to achieve this goal. For situations when exposures may exceed the RfD, the SAB stated that "it is unlikely that exposure of any populations to doses slightly over the RfD (even up to twice the RfD) would produce significant health effects." However, they seem to contradict this by advising that "if *total* exposures are at or higher than the RfD, then remedial actions may need to be considered." EPA disagrees with the idea that the conservative way in which the RfD is calculated automatically makes it unlikely that populations would experience "significant health effects" from exposures greater than the RfD. RfDs are not all equivalent in their derivation, and EPA believes multiple route exposures may be particularly important when the uncertainty factors associated with the RfD are small. Furthermore, the opinion that unless "*total* exposures [are] significantly in excess of the RfD, exposure from other routes should be neglected in calculations of AWQC" is counter to strong Agency directives to routinely consider and account for all routes of exposure when setting health-based criteria and with consideration to other regulatory activities. Despite arguments raised by SAB, EPA is recommending that only a portion of the RfD (or Pdp/SF)

be used in setting AWQC in order to account for other sources of exposure. EPA is also considering whether toxicity information (such as uncertainty factors, severity of effects, essentiality, possible additive/synergistic effects) should be considered in allocating the RfD or Pdp/SF. While combined exposures above the RfD or Pdp/SF may or may not be an actual health risk, a combination of health criteria exceeding the RfD or Pdp/SF may not be sufficiently protective. Therefore, EPA recommends routinely accounting for all sources and routes of non-occupational exposure when setting AWQC. EPA believes that maintaining total exposure below the RfD (Pdp/SF) is a reasonable health goal and that 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, along with other intake sources considered as background exposures) or in combination.

EPA has considered several alternative approaches to account for nonwater sources and to resolve past inconsistencies in setting criteria. Specifically, the Agency's Relative Source Contribution Policy Workgroup has considered six alternatives:

- Exposure Decision Tree Approach;
- Subtraction Approach;
- Percentage Approach;
- Tiered Approach;
- Safety Factor Approach; and
- Margin of Safety Approach.[14]

[14] This term refers to a method for accounting for nonwater sources of exposure and should not be confused with the nonlinear cancer assessment approach known as Margin of Exposure.

The Workgroup discussed, during the series of meetings, the various approaches to evaluating human exposure for regulatory and other risk assessment activities. Each approach has advantages and disadvantages that were discussed at length during these meetings, as do the basic concepts surrounding the subtraction and percentage methods of accounting for relevant exposures when allocating an RfD (Pdp/SF). The other four approaches are variations on the fundamental concepts of the subtraction or the percentage approaches.

Each of these six approaches is discussed in detail in a separate document contained in the public docket for this proposal (Borum, unpublished). The Agency recommends the Exposure Decision Tree Approach as described below. More detailed discussion and an example of how the Exposure Decision Tree is implemented are presented in the TSD.

As will become clear when reading the Exposure Decision Tree Approach, a typical evaluation will likely involve multiple sources/pathways of exposure and may involve more than one health-based criterion (either existing or in consideration for development). The current EPA policy discussions include the potential for applying this approach to other 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 (Pdp/SF) for criteria-setting purposes when appropriate.

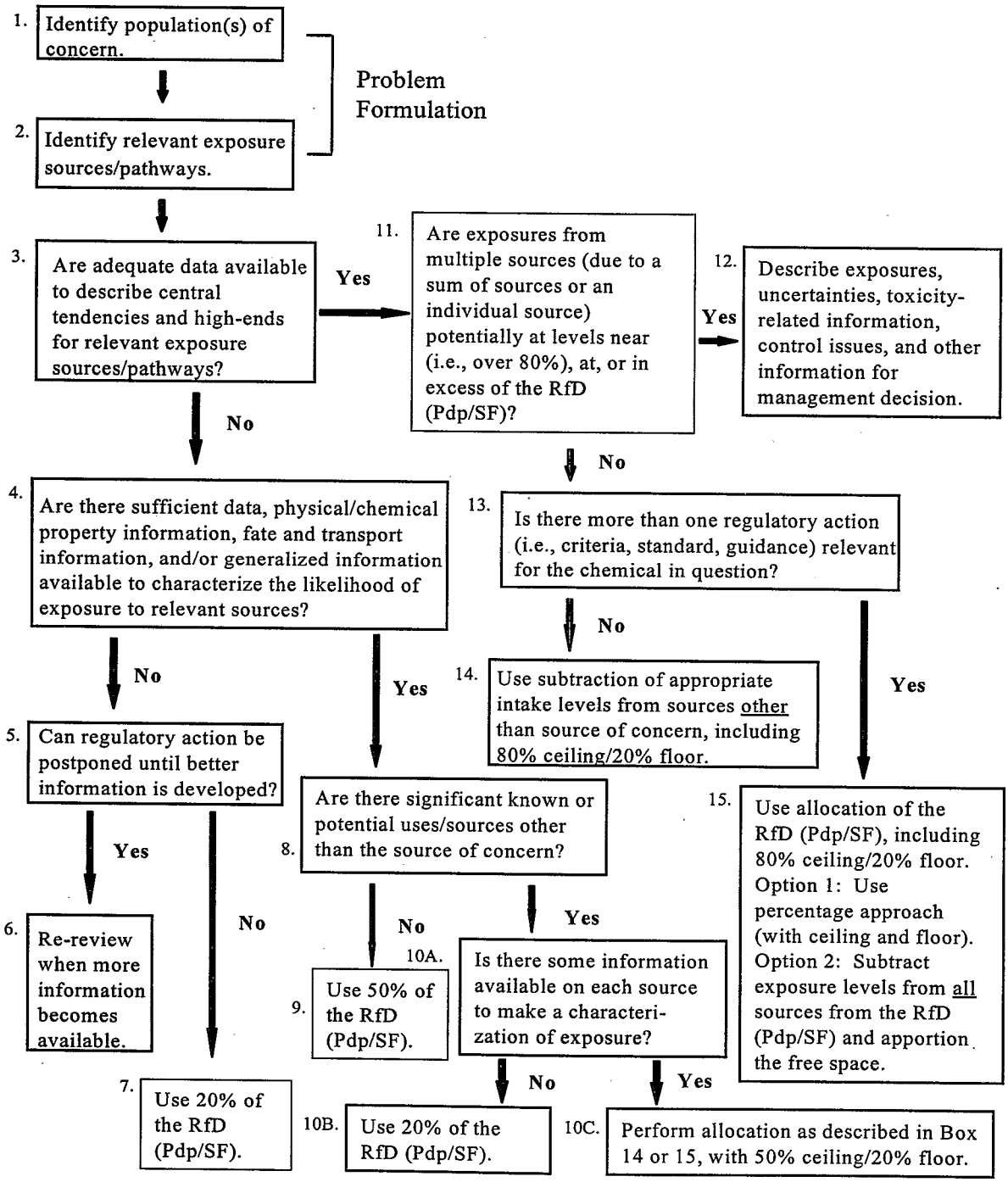
(b) Exposure Decision Tree Approach

The Exposure Decision Tree approach allows flexibility in the RfD (Pdp/SF) allocation among sources of exposure. When adequate data are available they are used to make accurate exposure predictions for the population(s) of concern. When this is not possible, a series of qualitative alternatives is proposed using less adequate data or default assumptions that allow for the inadequacies of the data while protecting human health. The decision tree allows for use of both subtraction and percentage methods of accounting for other exposures, depending on whether one or more health criterion is relevant for the chemical in question. 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). The decision tree (with numbered boxes) is shown in Figure IIIC-1. The underlying objective is to maintain total exposure below the RfD (Pdp/SF) while avoiding an extremely low limit in a single medium that represents just a fraction of the total exposure. To meet this objective, all proposed numeric limits lie between 80 percent and 20 percent of the RfD (Pdp/SF). EPA recommends use of the decision tree approach but also recognizes that departures from the approach may be appropriate in certain cases. The Agency endorses such action as long as reasons are given as to why it is not appropriate to follow the decision tree approach as long as the steps taken to evaluate the potential sources and levels of exposure are clearly indicated.

The first step in the decision process, problem formulation, is to identify the population(s) of concern (Box 1) and identify the relevant exposure sources and pathways (Box 2). The second step is to identify what data are available and whether they are adequate for calculating exposure estimates (Box 3). The term "data," as used here and discussed throughout the document, refers to ambient sampling data (from Federal, regional, State or area-specific studies) and not internal human exposure measurements. The adequacy of data is a professional judgment for each individual chemical of concern, but EPA recommends that the minimum acceptable data for Box 3 are exposure distributions that can be used to determine, with an acceptable 95 percent confidence interval, the central tendency and high-end exposure levels for each source. Once the two initial steps are complete, the next step depends on the type and quantity of data available.

Figure IIIC-1

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



If adequate data are available to describe the central tendencies and high-end levels from each exposure source/pathway, the levels of exposure are compared to the RfD or Pdp/SF (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 (Pdp/SF), then a 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 criterion, standard or other guidance being planned, performed or in existence for the chemical).

If the action under consideration is the sole action (i.e., multiple criteria, etc. are not relevant), then the recommended method for setting a health-based criterion is to use a subtraction calculation (Box 14). The criterion is the result after the appropriate intake levels from all other sources have been subtracted from the RfD (Pdp/SF). In addition, there is a ceiling on the amount of the RfD (Pdp/SF) available for allocation. This ceiling, 80 percent of the RfD (Pdp/SF), is 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. There is also a floor of 20 percent to prevent a *de minimis* exposure allocation in a particular medium.

If more than one regulatory action is relevant (as described above), then the recommended method for setting health-based criteria is to allocate the RfD (Pdp/SF) among those sources for which health-based criteria are being set (Box 15). Two main options for allocating the RfD (Pdp/SF) are presented in this Box. Option 1 for allocation 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. That is, 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 criterion would, in turn, be set at 50 percent of the RfD (Pdp/SF).

This option also uses an appropriate combination of intake values for each exposure source based on the variability in occurrence levels and determined on a case-by-case basis. Option 2 would involve subtracting from the RfD (Pdp/SF) the exposure levels from all sources of exposure 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, etc.); (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.

If the levels of exposure for the chemical in question are near (again, currently defined as greater than 80 percent), at, or in excess of the RfD (Pdp/SF), then the estimates of exposures and related uncertainties, potential allocations, toxicity-related information, control issues, and other information will be presented to managers for a decision (Box 12). The high levels referred to in Box 11 may be due to a single dominant source or to a combination of sources. The estimates of exposure performed in these instances and any allocations made would be done as described above

for Boxes 13, 14, and 15. However, because exposures that approach or exceed the RfD (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.

If the data fail the adequacy test (Box 3), any limited data that are available are evaluated (Box 4). This includes information about the chemical/physical properties, uses, environmental fate and transformation, limited sampling data that did not fulfill the requirements of Box 3, as well as any other information that would characterize the likelihood of exposure from various media for the chemical and aid in making a qualitative determination regarding the relation of one exposure source to another. Because these data are less certain (i.e., include information that does not directly measure exposure, or very limited data), criteria based on this information should be more conservative as shown in the remainder of the decision tree.

If there are not sufficient data/information to give any characterization of exposure, then 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, which has been used in past Agency water program regulations.

If there are sufficient data to give a characterization of exposure, the RfD (Pdp/SF) allocation depends on whether there are other known or potential uses or sources of concern (Box 8). If the source of concern is the sole source then EPA recommends an allocation of 50 percent of the RfD or Pdp/SF (Box 9). If there are multiple sources of concern and some information is available on each (Box 10A), the procedure, as shown in Box 10C, is the same as that in Box 14 or Box 15

depending on whether one or more criterion is relevant, but with a 50 percent ceiling to account for uncertainties from the limited amount of data (compared to Box 3). As with Box 11, if a determination is made in Box 10A (i.e., if information is available) that exposures are near, at or above the RfD (or Pdp/SF) based on the available information, the allocations made need to be presented to risk managers for decision. If information is lacking on some of the multiple exposure sources then EPA would use an allocation of 20 percent of the RfD or Pdp/SF (Box 10B).

(c) Quantification of Exposure

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. This is discussed in greater detail in the TSD (Section 2.3.3).

(d) Inclusion of Inhalation and Dermal Exposures From Household Drinking Water Uses

A number of drinking 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, thus, there is at least the possibility that some contaminants in water may be dermally absorbed.

Volatilization may increase exposure via inhalation and decrease exposure via ingestion and dermal absorption. The net effect of volatilization and dermal absorption upon total exposure to volatile drinking water contaminants 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 recommended methodology for explicitly incorporating inhalation (i.e., from volatilization) and dermal absorption exposures from household water uses in the derivation of health-based criteria. However, the Agency is supporting research in this area.

(e) Inclusion of Inhalation Exposures in RSC Analysis

The type and magnitude of toxicity produced may differ between routes; that is, the route of exposure can impact the effective concentration of a chemical and can also change the toxicity. For

example, an inhaled chemical such as hydrogen fluoride may produce local effects upon the lung that are not observed (or only observed at much higher doses) when the chemical is administered orally. Also, the active form of a chemical (and principal toxicity) can be the parent compound and/or one or more metabolites. With this Methodology, EPA recommends that differences in absorption and toxicity by different routes of exposure be determined and converted to reflect the differences in bioavailability and applied to the exposure assessment. EPA acknowledges that the issue of whether the doses received from inhalation and ingestion exposures are cumulative (i.e., toward the same threshold of toxicity) is complicated. Such a determination involves evaluating the chemical's physical characteristics, speciation and reactivity. A chemical may also exhibit different metabolism by inhalation versus oral exposure and may not typically be metabolized by all tissues. In addition, a metabolite may be much more or much less toxic than the parent compound. Certainly with a systemic effect, if the chemical enters the bloodstream, then there is some likelihood to contact the same target organ. Attention also needs to be given to the fact that both the RfD and RfC are derived based on the administered level. Toxicologists generally believe that the effective concentration of the active form of a chemical(s) at the site(s) of action determines the toxicity. If specific differences between routes of exposure are not known, it may be reasonable to assume that the internal concentration at the site from any route contributes as much to the same effect as any other route. A default of assuming equal absorption has often been used. However, for many of the chemicals that the Agency has reviewed, there is a substantial amount of information already known to determine differences in rates of absorption. For example, absorption, in part, is a function of blood solubility (i.e., Henry's Constant) and better estimations than the default can be made.

The RSC analyses that accompany these proposed Methodology revisions include consideration of inhalation exposures. Comment is requested on whether this is a reasonable approach to accounting for exposures for setting AWQC. Even if different target organs are involved between different routes of exposure, a conservative policy may be appropriate to keep all exposures below a certain level. One suggestion is to set allowable levels (via an equation) such that the total of ingestion exposures over the ingestion RfD in addition to the total of inhalation exposures over the inhalation RfC is not greater than 1 (Note: the RfD is typically presented in mg/kg-day and the RfC is in mg/m^3).

(f) 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 recommends using existing data on differences in bioavailability between water, air, soils, and different foods when estimating total exposure for use in allocating the RfD or Pdp/SF. The Agency has developed such exposure estimates for cadmium (USEPA, 1994). In the absence of data, EPA will assume equal rates of absorption from different routes and sources of exposure.

(g) Consideration of Non-water Exposure Procedures for Noncarcinogens, Linear Carcinogens, and Nonlinear Carcinogens

In the revised methodology, EPA recommends continuing to use the incremental risk approach that does not consider other exposure sources explicitly when setting AWQC for linear carcinogens. EPA recommends continuing to consider other exposure sources in setting AWQC for threshold toxicants, including both noncarcinogens and nonlinear carcinogens. Nonlinear carcinogens are discussed in detail in Appendix II, Section A.

3. Factors Used in the AWQC Computation

This section presents values for several exposure factors that are currently used in the derivation of AWQC. A new factor being considered by EPA, incidental ingestion from surface water, is also discussed in this Section, with a suggested default value.

When choosing exposure factors to include in the derivation of a criterion for a given pollutant, EPA recommends considering exposure factors relevant to populations that are most susceptible to that pollutant. In addition, highly exposed individuals should be considered when setting criteria. In general, exposure factors specific to adults and relevant to lifetime exposures are the most appropriate exposure factors to consider when determining criteria to protect against effects from long-term exposure. However, infants and children have a higher rate of water and food consumption per body weight compared to adults and also may be more susceptible to some pollutants than adults (USEPA, 1997c). In addition, exposure by pregnant women to certain toxic chemicals may cause developmental effects in the fetus (USEPA, 1997c). Exposures resulting in developmental effects may be of concern for some contaminants and should be considered along

with data applicable to long-term health effects when setting AWQC. (See Section B for further discussion of this issue.) Short-term exposure may include multiple or continuous exposures occurring over a week or so. Exposure factors relevant for considering chronic toxicity as well as exposure factors relevant for short-term developmental exposure concerns that could result in adverse health effects are discussed in the Sections below. States and Tribes may choose to develop criteria for developmental health effects based on exposure factors specific to children or to women of childbearing age.

EPA believes that the recommended exposure factor default intakes for adults with chronic exposure situations are adequately protective of the population over a lifetime. In providing additional exposure intake factors for women of childbearing age and children, EPA is providing flexibility for States and Tribes to establish criteria specifically targeted to provide additional protection to sensitive subpopulations (e.g., pregnant/nursing women, infants, children) or highly exposed subpopulations (e.g., sport anglers, subsistence fishers) using adjusted values for exposure parameters for body weight, drinking water intake, and fish consumption.

Each of the following Sections recommends exposure parameters for use in developing AWQC. These are based on both science policy decisions that consider the best available data, as well as risk management judgments regarding the overall protection afforded by their choice in the derivation of AWQC.

(a) Human Body Weight Values for Dose Calculations

(1) Rate Protective of Human Health from Chronic Exposure

The 1980 AWQC National Guidelines assumed a body weight of 70 kg for derivation of AWQC. EPA recommends maintaining the default body weight of 70 kg for calculating AWQC as a representative average value for both male and female adults. As stated above, exposure factors specific to adults are recommended to protect against effects from long-term exposure. This value is based on the following information. In an analysis of the NHANES II (the second National Health and Nutrition Examination Survey) data base, the 10th, 25th, and 50th percentile values for female adults 18-74 years old are 50.3, 55.4, and 62.4 kg, respectively (adapted from NCHS, 1987). For males in the same age range the comparable percentile values are 62.3, 68.7, and 76.9 kg, respectively. The mean body weight value for men and women ages 18 to 75 years old from this survey is 71.8 kg (adapted from NCHS, 1987). The mean value for body weight for adults ages 20-64 years old from another survey which primarily measured drinking water intake is 70.5 kg (Ershow and Cantor, 1989). The revised EPA Exposure Factors Handbook (USEPA 1997a) recommends 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 os used in the derivation of cancer slope factors and unit risks that appear in IRIS. Consistency is advocated between the dose-response relationship and exposure factors assumed.

(2) Rates Protective of Developmental Human Health Effects

As noted above, pregnant women may represent a more appropriate population for which to assess exposure from chemicals in ambient waters in some cases, because of the potential for developmental effects in fetuses. In these cases, body weights representative of women of childbearing age may be appropriate to adequately protect offspring from such health effects. 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 15-44 years old, taken from NHANES II (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 is 63.8 kg. Ershow and Cantor (1989) present body weight values specifically for pregnant women included in the survey; mean and median weights are 65.8 and 64.4 kilograms, respectively. Ershow and Cantor (1989), however, do not indicate the ages of these pregnant women. Based on this information for women of childbearing age and pregnant women, States may wish to use the mean body weight value of 65 kg in cases where pregnant women are the specific population of concern and the chemical of concern exhibits reproductive and/or developmental effects (i.e., the critical effect upon which the RfD or Pdp/SF is based). Using the 65 kg assumption would result in lower (more protective) criteria than criteria based on 70 kg.

As discussed earlier, because infants and children have a higher rate of water and food consumption per body weight compared to adults, a higher intake rate per body weight factor may be needed when comparing estimated exposure doses with critical doses when RfDs are based on health effects in children. To calculate these intake rates relevant to such effects, the body weight of children should be used. As with the default body weight for pregnant women, EPA is not

recommending the development of additional AWQC (i.e., similar to drinking water health advisories) that focus on acute or short-term effects since these are not seen routinely as having a meaningful role in the water quality criteria and standards program. However, there may be circumstances where the consideration of exposures for these groups is warranted. Although the AWQC are generally based on chronic health effects data, they are intended to also be protective with respect to adverse effects that may reasonably be expected to occur as a result of elevated shorter-term exposures. EPA acknowledges this as a potential course of action and is, therefore, recommending these default values for States and Tribes to utilize in such situations.

EPA is recommending an assumption of 28 kg as a default body weight to calculate AWQC to provide additional protection for children when the chemical of concern indicates health effects in children are of predominant concern (i.e., test results show children are more susceptible due to less developed immune systems, neurological systems, and/or lower body weights). The value is based on the mean body weight value of 28 kilograms for children ages 0-14 years old, which combines body weight values for individual age groups within this larger group. The mean value is based on body weight information from NHANES II (NCHS, 1987) for individual-year age groups between 6 months and 14 years old, and weights the values for these different ages by current population percentages (from U.S. Bureau of the Census, 1996) to represent a body weight value applicable to the current population of children aged 0-14 years. The same mean body weight of 28 kilograms is also obtained using body weight values from Ershow and Cantor (1989) for five age groups within this range of 0-14 years, and applying the above weighting method. The 28 kg assumption is also consistent with the estimated fish intake rates proposed for children in the same age range. Unfortunately, fish intake rates for finer age group divisions are not possible due to the

limited sampling base from the fish intake survey; there is limited confidence in calculated values (e.g., the mean) for such fine age groups. Given this limitation, the broad age category of body weight for children is suitable for use with the default fish intake assumption.

Given the hierarchy of preferences regarding the use of fish intake information [see Section C.3.(d)], States may have more comprehensive data and prefer to target a more narrow, younger age group. If States choose to specifically evaluate infants and toddlers, EPA would recommend 10 kg as a default body weight assumption for water intake for children ages 1-3 years old, as has been used in other EPA water programs. The 10th, 25th, and 50th percentile values of body weight 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). Based on an analysis of the NHANES II data base reported in the EPA's Exposure Factors Handbook, the 10th, 25th, and 50th percentile values for children less than 3 years old are 8.5, 9.6, and 11.3 kg for females, and 9.1, 10.3, and 11.8 kg for males, respectively (USEPA, 1989). The mean for both sexes from NHANES II is 11.6 kg. The 10 kg body weight assumption is representative of the majority of children under the age of 3. As with the 28 kg assumption, EPA recommends a more protective body weight assumption than the median value because of the increased susceptibility of infants and toddlers to acute effects from water-based formula intake.

Body weight values for individual ages within the larger range of 0-14 years are listed in the TSD for this Notice for those States and Tribes who wish to use body weight values for these individual groups. States and Tribes may wish to consider certain general developmental ages (e.g., infants, pre-adolescents, etc.), or certain specific developmental landmarks (e.g., neurological development in the first four years), depending on the chemical of concern. EPA encourages States

and Tribes to choose a body weight intake from the tables presented in the TSD, if they believe a particular age subgroup is more appropriate.

(3) Rates Based on Combining Intake and Body Weight

As discussed below, EPA is also soliciting comments on whether intake assumptions should be given on a per kg body weight basis. Under this alternate approach, default body weight assumptions of 10, 28, 65, or 70 kg are not needed because the approach involves dividing individual respondents' intake rates (determined in surveys of drinking water or fish intake) by their own self-reported body weights.

(b) Drinking Water Intake Rates

(1) Rate Protective of Human Health from Chronic Exposure

The 1980 AWQC National Guidelines assumed a water intake rate of 2 L/day. There is comparatively little variability in water intake within the population, compared to fish intake (i.e., drinking water intake varies, by and large, by about a three-fold range, whereas fish intake can vary by 100-fold). The 50th, 75th, and 90th percentile values for adults 20 - 64 years old are 1.3, 1.7, and 2.3 L/day, respectively (Ershow and Cantor, 1989). The 2 L/day value represents the 84th percentile for adults from the Ershow and Cantor study. EPA recommends maintaining the default tap water intake rate of 2 L/day. Individuals who work or exercise in hot climates could have water consumption rates significantly above 2 L/day, and EPA believes that States and Tribes should

consider regional or occupational variations in water consumption. EPA believes that the 2 L/day assumption is representative of a majority of the population over the course of a lifetime. This assumption was used with the 1980 methodology and has also been used in EPA's drinking water program. Although a policy decision, 2 L/day is a reasonable and protective determination that represents the intake of most water consumers in the general population according to available drinking water studies, as summarized above and described in greater detail in the TSD. EPA believes that this assumption continues to represent an appropriate risk management decision.[15] Based on the study data, EPA also recommends 2 L/day for women of childbearing age.

(2) Rate Protective of Developmental Human Health Effects

As noted above, because infants and children have a higher water consumption per body weight compared to adults, a water consumption rate indicative of children is proposed for use when RfDs are based on health effects in children. Use of this water consumption rate should result in adequate protection for infants and children when setting criteria based on health effects for this target population. Estimating a mean drinking water intake for children ages 0-14 years old, combining 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 recommends a drinking water intake of 1 L/day to, again, represent a majority of the population in this age group. This value is equivalent to about the

[15] EPA is currently conducting an analysis to generate estimates of water intake based on recent data from the USDA's CSFII. Estimates will be generated by population demographics including, age, gender, race, socioeconomic status and geographical region. Results of this analysis may be considered in the future with this methodology.

75th percentile value, which is 960 ml, for children ages 1-10 years old (Ershow and Cantor, 1989). The 50th, 75th, and 90th percentile values for children 1-3 years old are 0.6, 0.8, and 1.2 L/day, respectively (Ershow and Cantor, 1989).

(3) Rates Based on Combining Drinking Water Intake and Body Weight

As an alternative to considering body weight and drinking water intake rates separately, EPA is considering using the actual intake per body weight data that is available in the Ershow and Cantor (1989) report. This approach has the advantage of using self-reported body weights of survey respondents, instead of converting to the 70 kg or 10 kg default assumptions. These alternate values are presented in Ershow and Cantor (1989) or can be determined from Ershow and Cantor (1989) and U.S. Bureau of the Census (1996) using the methods described above to determine a weighted mean. For example, the mean, 50th, 75th, and 90th percentile values of tap water intake for adults 20-64 years old are 19.9, 18.2, 25.3, and 33.7 ml/kg body weight, respectively. Using information from Ershow and Cantor (1989) for fine age categories, the weighted mean intake for children ages 0-14 years old is 32.6 ml/kg, and using the same weighting procedure, the approximate 50th, 75th, and 90th percentiles for this age group are 28.6, 42.3, and 59.3 ml/kg. The 50th, 75th, and 90th percentile values of tap water intake for children 1-3 years old are 41.4, 60.4, and 82.1 ml/kg body weight, respectively. It should be noted that in their 1993 review, SAB felt that using drinking water intake rate assumptions on a per body weight basis would be more accurate, but did not believe this change would appreciably affect the criteria values.

(c) Incidental Ingestion from Ambient Surface Waters

To prevent potential health risks from incidental recreational ingestion, an incidental intake rate is necessary. EPA recommends using 10 ml/day as the chronic incidental ingestion rate. The value would be divided by the adult body weight of 70 kg. This chronic intake is based on information about the amount of water that may be ingested in a given hour of recreational exposure to water (30 ml) multiplied by the number of hours of recreational water use throughout a year and averaged over the year to obtain an average intake per day. (Refer to the TSD for further explanation.) As stated earlier, this intake would only be used in those cases where the waterbody is not used for potable water (e.g., estuaries) and criteria are based solely on fish ingestion. When developing criteria for waterbodies that are potential drinking water sources, the assumption of 2 L/day of direct ingestion is likely to account for the additional possible ingestion via recreational activities and, therefore, this incidental rate will not be added.

(d) Fish Intake Rates

(1) Rates Protective of Human Health from Chronic Exposure

When deriving AWQC, EPA strives to provide adequate protection [as described earlier in Section C.1.(a)(1), Policy Issues] from adverse health effects to highly exposed populations such as recreational and subsistence fishers as well as the general population. Based on available studies that characterize consumers of fish, recreational fishers and subsistence fishers appear to be two distinct groups whose intake rates are greater than the general population. It is, therefore, EPA's decision

to discuss intakes for these two groups, in addition to the general population. Because the level of fish intake in highly exposed populations varies by geographical location, EPA suggests a four preference hierarchy for deriving consumption rates that encourages use of the best local, State, or regional data available but provides a default rate based on national statistics if there are no other data. A thorough discussion of the development of this policy method and relevant data sources is contained in the TSD. The four preference hierarchy is: 1) use of local data; 2) use of data reflecting similar geography/population groups; 3) use of data from national surveys; and 4) use of proposed default intake rates.

The recommended four preference hierarchy is intended for use in evaluating fish intake from 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 or dietary value (DT in the 1980 methodology equation). Refer to the TSD for further discussion. States and Tribes need to ensure that when evaluating overall exposure to a contaminant, marine fish intake is not double-counted with the other dietary intake estimate used. Coastal States and Tribes that believe accounting for total fish consumption (i.e., fresh/estuarine and marine species) is more appropriate for protecting the population of concern may do so, provided that the marine intake component is not double-counted with the RSC estimate. 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 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.

EPA's first preference is that States and Tribes use the results from fish intake surveys of local watersheds within the State to establish fish intake assumptions that are representative of the defined populations being addressed for the particular waterbody. Again, EPA recommends that data indicative of fresh/estuarine species only be used which is, by and large, most appropriate for developing AWQC. EPA also recommends the use of cooked weight intake values which is discussed in greater detail with the fourth preference. States and Tribes may use either high-end values (such as the 90th or 95th percentile values) or central tendency values (mean or medians) for an identified population that they plan to protect (e.g., subsistence fishers or sport fishers). The mean or median value should be the lowest value considered by States or Tribes when choosing intake rates for use in criteria derivation. Furthermore, when considering median values from fish consumption studies, States and Tribes need to ensure that the distribution is based on survey respondents who reported consuming fish because surveys based on both consumers and nonconsumers typically result in median values of zero. If a State or Tribe chooses values (whether the central tendency or high-end values) from studies that particularly target high-end consumers, these values should be compared to high-end fish intake rates for the general population to make sure that the high-end consumers within the general population would be protected by the chosen intake rates. EPA believes this is a reasonable procedure and is also consistent with recent water quality guidance established for the Great Lakes. (See FR vol. 60, No. 56, Thursday, March 23, 1995). States and Tribes may wish to conduct their own surveys of fish intake, and EPA guidance is available on methods to conduct such studies in *Guidance for Conducting Fish and Wildlife Consumption Surveys* (USEPA, 1997b). Results from broader geographic regions in which the State or Tribe is located can also be used, but may not be as applicable as results from local watersheds. Since such studies would ultimately form the basis of a State or Tribe's AWQC, EPA would review

any surveys of fish intake for consistency with the principles of EPA's guidance, as part of the Agency's review under 303(c).

If surveys conducted in the geographic area of the State or Tribe are not available, EPA's second preference is that States and Tribes consider results from existing fish intake surveys that reflect similar geography and population groups (e.g., from a neighboring State or Tribe or a similar watershed type), and follow the method described above regarding target values to derive a fish intake rate. Again, EPA recommends the use of cooked weight intake values and the use of fresh/estuarine species data only. Results of existing local and regional surveys are discussed in greater detail in the TSD.

If applicable consumption rates are not available from local, State, or regional surveys, EPA's third preference is that States and Tribes select intake rate assumptions 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). The CSFII, conducted annually by the USDA, collects food consumption information from a probability sample of the population of the 48 conterminous states. Respondents to the survey provide three days of dietary recall data. A detailed description of the combined 1989-1991 CSFII survey, the statistical methodology, and the results and uncertainties of the EPA analyses are provided in USEPA (1998). The TSD for this Notice presents selected results from this report including point and interval estimates of combined finfish and shellfish consumption for the mean, 50th (median), 90th, 95th, and 99th percentiles. The estimated fish consumption rates are by fish habitat (i.e., freshwater/estuarine, marine and all habitats) for the following population groups: (1)

all individuals; (2) individuals age 18 and over; (3) women ages 15-44; and (4) children age 14 and under. Three kinds of estimated fish consumption rates are provided: (1) per capita rates [i.e., rates based on consumers and nonconsumers of fish (from the survey period. Refer to the TSD for further discussion)]; (2) acute consumption rates (i.e., rates based on respondents who reported consuming finfish or shellfish during the three-day reporting period); and (3) per capita consumption by body weight (i.e., per capita rates reported as milligrams of fish per kilogram of body weight per day).

In addition, the TSD presents estimated per capita finfish and shellfish consumption rates for nine geographical regions of the U.S. based on the 1989-1991 CSFII. States and Tribes may wish to use these regional values if they do not have significant tier one or tier two data but do have limited regional data, and if they believe that the consumption rates of the particular population of concern differ from the national rates. The TSD also discusses precautions regarding their use due to limitations in the data set. Similarly, if a State or Tribe has not identified a separate well-defined population of high-end consumers and believes that the national data from the CSFII are representative, they may choose these rates.

EPA's fourth preference is that States and Tribes use as fish intake assumptions the following default rates, based on the 1989-1991 CSFII data, that EPA believes are representative of fish intake for different population groups: 17.80 g/day for the general adult population and sport fishers, and 86.30 g/day for subsistence fishers. These are risk management decisions that EPA has made after evaluating numerous fish intake surveys. These values represent the intake of freshwater/estuarine finfish and shellfish as consumed. As with the other preferences, EPA requests that States and Tribes routinely consider whether there is a substantial population of sport fishers or subsistence

fishers when developing site-specific estimates, rather than automatically basing them on the typical individual. Because the combined 1989-1991 CSFII survey is national in scope, EPA proposes that the results from this survey be used to estimate fish intake for deriving national criteria. EPA has recognized the data gaps and uncertainties associated with the analysis of the CSFII in the process of making its default recommendations. The estimated mean of freshwater and estuarine fish ingestion for adults is 5.6 g/day, and the median is 0 g/day. The estimated 90th percentile is 17.80 g/day; the estimated 95th percentile is 39.04 g/day; and the estimated 99th percentile is 86.30 g/day. The median value of 0 g/day may reflect the portion of individuals in the population who never eat fish as well as the limited reporting period (3 days) over which intake was measured. By applying as a default 17.8 g/day for the general adult population, EPA intends to select an intake rate that is protective of a majority of the population (again, the 90th percentile of consumers and nonconsumers according to the CSFII survey data). EPA further considers this rate to be indicative of the average consumption among sport fishers based on averages in the studies reviewed, which are presented in the TSD. Similarly, EPA believes that the assumption of 86.30 g/day is within the range of average consumption estimates for subsistence fishers based on the studies reviewed. The 95th percentile value, 39.04 g/day, is also within the range of average consumption for subsistence fishers, although on the low end according to the studies reviewed. The 1992 National Workshop experts acknowledged that the high-end values are representative of rates for highly exposed groups such as subsistence fishermen, specific ethnic groups, or other high-risk people. EPA is aware that some local and regional studies indicate greater consumption among Native American, Pacific Asian American, and other subsistence consumers and recommends the use of those studies in appropriate cases, as indicated by the first and second preferences.

The estimated values derived from the combined 1989-1991 CSFII survey can be compared with the default values in the 1980 AWQC National Guidelines. The 1980 AWQC National Guidelines recommended a fish intake rate of 6.5 g/day. This value was based on the mean per capita consumption rate of freshwater and estuarine finfish and shellfish from 30-day diary results that were reported in the 1973 - 1974 National Purchase Diary Survey. It is generally believed that the consumption of fish has increased somewhat in recent years due to nutritional and other preferential choices. When comparing the old default rate of 6.5 g/day with the new arithmetic mean indicated above (5.6 g/day), the use of cooked weights and the redesignation of certain species (as described in the TSD) must be kept in mind.

As indicated above, the default intake values proposed, as well as the rest of the CSFII values presented in the TSD tables, are based on the cooked weights of the fish analyzed, which was the basis of the survey design. There has been some question regarding whether to use cooked or uncooked weights of fish intake for deriving the AWQC. Studies show that, typically, with a filet or steak of fish, the weight loss in cooking is about 20 percent; that is, the uncooked weight is approximately 20 percent higher (Jacobs et al., 1998). This obviously means that using cooked weights results in a slightly lower intake rate and slightly less stringent AWQC. In researching consumption surveys for this proposal, EPA has found that some surveys have reported rates for cooked fish, others have reported uncooked rates, and many more are unclear as to whether cooked or uncooked rates are used.

There are several issues regarding whether to use cooked or uncooked weights when estimating fish consumption rates. The first issue concerns the effect of the cooking process on the

concentration of the toxicant in the fish tissue. For example, if in the cooking process, the mass of a toxicant in the fish tissue remains constant, then the concentration in the fish tissue will increase (the weight of the fish tissue decreases). This appears to be the case with a chemical such as mercury because it binds strongly to proteins and, thus, concentrates in the muscle tissue (Minnesota Department of Health, 1992). However, as has been seen with numerous organic chemicals (e.g., PCBs), some cooking processes tend to decrease the mass of toxicant, thus reducing the concentration in the fish tissue (Zabik, et al., 1993). Of importance here is that the mass of the contaminant in the fish tissue stays constant or is reduced. Unfortunately, there are rather few chemicals for which measurements are available. This issue is complicated further by the fact that different chemicals accumulate in different parts of the fish; that is, some chemicals accumulate in the muscle tissue, some in the gills, some in the viscera, etc. Therefore, the method of preparation (i.e., cleaning and trimming) can greatly affect the potential intake of the contaminant, as can the cooking method and the considerable variation in both of these factors between species of fish. In addition, there is the relatively unexplored area of how the cooking process affects the nature of the chemical. Specifically, the cooking process may change the "parent" compound to a by-product, or form a different compound altogether.

Nevertheless, the cooked weight values are consistent with the recent Great Lakes guidance (which was specifically based on studies describing consumption rates of cooked fish) and, by and large, cooked fish is what people consume. This is also consistent with non-fish dietary estimates made by both EPA's pesticide program and FDA's Total Diet Study program. That is, their analyses are based on prepared foods, not raw commodities. However, EPA's *Guidance For Assessing Chemical Contaminant Data For Use In Fish Advisories* recommends analysis and advisories based

on uncooked fish (USEPA, 1997c). States and Tribes should have the flexibility to consider raw fish consumption if they believe that the population they are targeting are consumers of raw fish. It should be noted that any raw shellfish consumed by respondents in the CSFII survey is included in the "as consumed" values. EPA cautions States and Tribes that the as consumed weights provided are not to be used for developing fish advisories, which is a substantially different program than the water quality criteria program.

Therefore, EPA recommends using cooked weight intake rates, as they better reflect the potential exposure from fish consumption versus using the uncooked weights. If States and Tribes find that, when using site-specific or regional data, they are limited to data for uncooked weights only, they may choose to use these data in their calculations, provided that they adjust for the weight loss in cooking (i.e., by reducing the value by 20 percent). If a State or Tribe believes that the population of concern is preparing fish in such a manner that the amount normally lost is actually consumed as well, then they may consider using the uncooked weight. In addition, EPA recommends assuming no change in contaminant concentration from cooking as a default. If information on chemical change from cooking is available, then States are encouraged to use this information. If a State or Tribe has information on chemical change from cooking, they may consider using a cooking loss factor to adjust the BAF accordingly.

It should be noted that there has been a redesignation of several species from how they were classified in the 1973-74 National Purchase Diary Fish Consumption Survey. Most significantly, salmon has been reclassified from a freshwater/estuarine species to a marine species. As marine harvested salmon represents approximately 99 percent of salmon consumption, removal reduces the

overall fresh/estuarine fish consumption rate by 13 percent. Although they represent a very small percentage of freshwater/estuarine intake, land-locked and farm-raised salmon are still included. The basis for this decision is that the majority of the life span of all species of salmon (except land-locked and farm-raised populations) is spent in marine waters. This includes most of the species' growth phase, including the pre-spawning food gorging that the fish undertake. For the actual spawning event, most salmon fast, thus spending their energy making the trip to their spawning destination. This rationale is explained more fully, with citations, in the TSD. All of the species apportionments are indicated in Appendix A of the TSD (Tables A.31 through A.34) in parenthesis by the species name. The 13 percent reduction described above for salmon can be calculated via these tables.

(2) Rates Protective of Developmental Human Health Effects

Exposures resulting in health effects in children or developmental effects in fetuses may be of primary concern. As discussed at the beginning of Section C.3, depending on the type of exposure or effect, States and Tribes may wish to use exposure factors for children or women of childbearing age in these situations. As stated previously, EPA is not recommending the development of additional AWQC but is acknowledging that basing a criterion on these population groups is a potential course of action and is, therefore, proposing the following default intake rates for States and Tribes to utilize in such situations.

Since children have a higher fish consumption per body weight compared to adults, using a higher fish consumption rate per body weight may be needed for setting AWQC to assure adequate protection for children. EPA's preferences for States and Tribes in selecting assumptions for intake

rates relevant for children is the same as that discussed above for establishing assumptions for average daily consumption rates for chronic effects, i.e., in order of decreasing preference, results from fish intake surveys of local watersheds, results from existing fish intake surveys that reflect similar geography and population groups, the distribution of intake rates from nationally based surveys (e.g., the CSFII), or finally, the default rate that EPA recommends below that is representative of a selected population group. The TSD for this Notice will present some distributional values related to the intake values relevant for assessing exposure when health effects to children are of concern. When an RfD is based on health effects in children, EPA recommends a default intake rate of 108.36 g/day for assessing those contaminants that exhibit adverse effects. This is equivalent to about the 90th percentile consumption rate for actual consumers of freshwater/estuarine finfish and shellfish for children ages 14 and under using the combined 1989-1991 results from the CSFII survey. The value was calculated based on data for only those children who ate any fish during the 3-day survey period, and the intake was averaged over the number of days during which fish was actually consumed. EPA believes that by selecting the data for consumers only, the 90th percentile is a reasonable intake rate to use in assessments for effects where children are of primary concern. As discussed previously, EPA is recommending a default body weight of 28 kg to address such potential effects from fish consumption by children. EPA is providing these intake assumption values for States and Tribes that choose to provide additional protection when developing criteria that they believe should be based on health effects in children. This is consistent with the rationale in the recent guidance established for the Great Lakes (as already cited) and is an approach that EPA believes is reasonable.

There are also cases in which pregnant women may be the population of most concern, due to the possibility of developmental effects that may result from exposures of the mother to toxicants. In these cases, fish intake rates specific to females of childbearing age are most appropriate when assessing exposures to developmental toxicants. When an RfD is based on developmental toxicity, EPA proposes a default intake rate of 148.83 g/day for assessing exposures for women of childbearing age from contaminants that cause developmental effects. This is equivalent to about the 90th percentile consumption rate for actual consumers of freshwater/estuarine finfish and shellfish for women ages 15-44 using the combined 1989-1991 results from the CSFII survey. As with the rate for children, this value represents only those women who ate fish during the 3-day survey period. As discussed previously, EPA is recommending a default body weight of 65 kg for women of childbearing age.

(3) Rates Based on Combining Fish Intake and Body Weight

As an alternative to looking at fish intake values separately from body weight, EPA is considering using the actual intake per body weight data. This approach has the advantage of using actual body weights of survey respondents, instead of converting to the 70 kg, 65 kg, 28 kg, or 10 kg default assumptions. In its 1993 review, SAB felt that using fish intake rate assumptions on a per body weight basis would be more accurate, but did not believe this change would appreciably affect the criteria values.

4. Request for Comments

1. EPA requests comment on the choice of population to protect and on the adequacy of their assumptions in protecting this population.

2. EPA requests comment on the Agency's recommendation to include the drinking water pathway explicitly in deriving the AWQC for the protection of human health where drinking water is a designated use.

3. EPA requests comment on the Agency's recommendation to continue the practice of setting AWQC that account for combined drinking water and fish consumption, as well as a separate criterion for fish/shellfish consumption alone.

4. EPA requests comment on whether AWQC based only on fish ingestion (or aquatic life criteria) adequately protect recreational users from health effects resulting from incidental ingestion from water bodies not considered sources of potable water (e.g., estuaries).

5. EPA requests comment on the Agency's recommendation to include incidental ingestion in the calculation of AWQC in those cases where the water body is not used for potable water.

6. EPA requests comment on the Agency's recommendation that only a portion of the RfD be used in setting AWQC in order to account for other sources of exposure.

7. The Agency also requests comment on whether toxicity information (such as uncertainty factors, severity of effects, essentiality, and possible additive/synergistic effects) should be considered in allocating the RfD.

8. EPA requests comment on the choice of the Exposure Decision Tree approach and the choice of the 80 percent ceiling and 20 percent floor as bounding levels for the RfD allocation. The Agency also requests comment on the use of the subtraction approach and the percentage approach within the decision tree.

9. EPA requests comment on how inhalation and dermal absorption exposures from water should be estimated and included in calculating health-based criteria.

10. EPA requests comment on the appropriateness of including inhalation exposures when accounting for other sources of exposure in setting AWQC.

11. EPA requests comment on the Agency's recommendation to use existing data on differences in bioavailability between water, air, soils, and different foods when estimating total exposure for use in allocating the RfD. In the absence of such data, EPA will assume equal rates of absorption from different routes and sources of exposure. EPA requests comment on this assumption.

12. EPA requests comment on the Agency's recommendation to continue using the incremental risk approach that does not consider other exposure sources explicitly when setting

AWQC for linear carcinogens, and to continue using other exposure sources in setting AWQC for threshold toxicants including noncarcinogens and nonlinear carcinogens.

13. EPA requests comment on whether a default body weight of 65 kg should be used in cases where pregnant women constitute the target population.

14. EPA requests comment on the Agency's proposal to use 28 kg as the default body weight to calculate AWQC which protects against adverse effects in children when the chemical of concern has an RfD based on health effects in children.

15. EPA requests comment on whether 10 kg or a different body weight should be used as the default assumption to calculate AWQC for children's health effects from water intake for children 1-3 years old, as has been used in other EPA water programs.

16. EPA requests comment on whether additional default body weights should be developed for finer age categories due to the consideration of different developmental stages.

17. EPA requests comment on whether to use separate tap water intake and body weight assumptions (e.g., 2 L/day, 70 kg body weight) or assumptions that combine tap water intake and body weight (e.g., 30 ml tap water/kg body weight), and what values should be used.

18. Although EPA is not recommending an incidental ingestion rate for derivation of criteria based on short-term health effects at this time, the Agency requests comment on the use of an intake

of 30 ml/hour in cases where shorter-term effects may be considered in the derivation of criteria. (EPA assumes that this 30 ml incidental rate may be ingested by children, and thus for RfDs based on health effects in children, this value may be divided by the lower body weights of children to adequately protect them from health effects resulting from incidental ingestion.)

19. EPA requests comment on (1) the use of the CSFII survey results in setting national criteria given the known limitations (i.e., the 3-day reporting period); (2) whether EPA should select default rates for different population groups, including 17.80 g/day for sportfishers and 86.30 g/day for subsistence fishers in addition to the value of 17.80 g/day for the typical adult individual (EPA also requests comment on alternatively using 39.04 g/day for subsistence fishers); and (3) which default intake rate(s) should be used in setting criteria. With regard to the default alternative for subsistence fishers, EPA requests comment on which is more indicative of fresh/estuarine consumption rates among the population group.

20. EPA requests comment on the use of cooked versus uncooked fish intake weights, the concepts of mass and concentration of a toxicant in fish tissue and the potential changes from cooking, as well as the potential changes in the structure of the toxicant.

21. EPA requests comments on the rationale for redesignating salmon as a marine species, as well as the rationale for the other species designations.

22. EPA requests comments on the use of the default rate of 108.36 g/day of fish intake for children when assessing effects from contaminants that are based on health effects in children. EPA

similarly requests comments on the use of the default intake rate of 148.83 g/day for women of childbearing age when assessing exposures from contaminants that cause developmental effects.

23. EPA requests comments on whether to use separate fish intake and body weight assumptions (e.g., 17.80 g/day, 70 kg body weight) or assumptions that combine fish intake and body weight (e.g., 254.3 mg fish/kg body weight), and what values should be used.

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D. Bioaccumulation

1. Introduction

Aquatic organisms can accumulate certain types of chemicals in their bodies when exposed to these chemicals in water, food, and other sources. This process is called bioaccumulation. For some chemicals, uptake through the food chain is the most important route of exposure. As lower trophic level organisms are consumed by higher trophic level organisms, the tissue concentrations of these chemicals may increase with each trophic level so that chemical residues in top carnivores may be many orders of magnitude greater than the concentration of the chemical in the environment.

Although ambient concentrations of certain chemicals in the environment may be too low to affect the lowest level organisms, this biomagnification process can result in concentrations which may pose severe health risks to the consumers of top trophic level aquatic organisms.

In order to properly account for potential human exposure to waterborne contaminants, human health ambient water quality criteria should be developed based on principles of bioaccumulation. The degree to which chemicals bioaccumulate can vary widely (spanning several orders of magnitude) for different chemicals. Thus, if two chemicals are equal in every respect except for the extent to which they bioaccumulate, the chemical with the higher bioaccumulation factor (a measure of bioaccumulation) will have the lower water quality criterion. Prior to deriving a human health water quality criterion, the extent of bioaccumulation for the chemical of interest must be established.

2. 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 and applying these principles in real world situations, such as the derivation of AWQC. 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 a water concentration which is not averaged over a sufficient time period 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 (BAF) is defined in this Notice 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.

3. Existing EPA Guidance

In developing criteria to protect humans from the consumption of contaminated aquatic organisms, EPA has relied upon the BCF and occasionally BAF to relate water concentrations to the amount of a contaminant that is ingested.

BCFs are determined either by measuring bioconcentration in laboratory tests (comparing fish tissue residues to chemical concentrations in test waters), or by predicting the BCF from a chemical's octanol-water partition coefficient (K_{ow} or P). The log of the octanol-water partition coefficient (log K_{ow} or log P) has been shown to be empirically related to the log of the BCFs (e.g., Mackay, 1982; Connell, 1988; Veith et al., 1979), as described further by the equations below.

The 1980 AWQC National Guidelines for deriving human health criteria allowed for the use of laboratory-measured or predicted BCFs when the preferred field-measured BCFs (equivalent to field-measured bioaccumulation factors (BAFs) described below) were not available. In those cases

where an appropriate laboratory-measured BCF was not available, the equation "log BCF = (0.85 log K_{ow}) - 0.70" was used (Veith et al., 1979) to estimate the BCF for aquatic organisms.

In 1991, EPA issued the final "Technical Support Document for Water Quality-Based Toxics Control" (EPA 505/2-90-001) and a draft document entitled "Assessment and Control of Bioconcentratable Contaminants in Surface Waters" for notice and comment (56 FR 13150). These documents, relying on additional research into the relationship between BCF and log K_{ow}, recommend that a slightly different equation be used to derive BCFs in the absence of laboratory-measured BCFs (Veith and Kosian, 1983; log BCF = 0.79 log K_{ow} - 0.40).

EPA's 1991 National guidance documents, the "Technical Support Document for Water Quality-Based Toxics Control" and draft "Assessment and Control of Bioconcentratable Contaminants in Surface Waters," recommend a methodology for estimating the BAF where there is an absence of a field-measured BAF. This methodology multiplies the laboratory-measured or predicted BCF by a factor which accounts for the biomagnification of a pollutant through trophic levels in a food chain. As larger predatory aquatic organisms (e.g., salmon) consume other fish and aquatic organisms, the amount of some contaminants in the consumed fish is concentrated in the predator. The factor which accounts for this biomagnification through the food chain is called the food chain multiplier (FCM) in these 1991 National guidance documents. EPA calculated the FCMs using a model of the step-wise increase in the concentration of an organic chemical from phytoplankton (trophic level 1) through the top predatory fish level of a food chain (trophic level 4) (Thomann, 1989).

The FCMs were determined by first running Thomann's model to generate BCFs and BAFs for trophic level 2, and BAFs for trophic levels 3 and 4. This was done for a range of log K_{ow} values from 3.5 to 6.5, at intervals of a tenth of log K_{ow} value. Second, the FCMs for each log K_{ow} value in this range were calculated using the following equations:

For trophic level 2 (zooplankton):

$$\text{FCM for Trophic Level 2} = \frac{\text{BAF2}}{\text{BCF2}}$$

For trophic level 3 (small fish):

$$\text{FCM for Trophic Level 3} = \frac{\text{BAF3}}{\text{BCF2}} \qquad \text{(Equation IIID-1)}$$

For trophic level 4 (top predator fish):

$$\text{FCM for Trophic Level 4} = \frac{\text{BAF4}}{\text{BCF2}} \qquad \text{(Equation IIID-2)}$$

Where BCF2 is the BCF for trophic level 2 organisms, and BAF2, BAF3, and BAF4 are the BAFs for trophic levels 2, 3, and 4, respectively.

On March 23, 1995 (60 *FR* 15366), EPA promulgated the Great Lakes Water Quality Initiative (GLWQI or GLI) guidance. The GLWQI guidance incorporated BAFs in the derivation of criteria to protect human health because it is believed that BAFs are better predictors of chemical

concentrations in fish tissue than BCFs since BAFs include consideration of contaminant uptake from all routes of exposure (i.e., which occurs in field situations). The final GLWQI guidance established a hierarchy of four methods for deriving BAFs for nonpolar organic chemicals: (1) field-measured BAFs; (2) predicted BAFs derived using a field-measured biota-sediment accumulation factor (BSAF); (3) predicted BAFs derived by multiplying a laboratory-measured BCF by a food chain multiplier; and (4) predicted BAFs derived by multiplying a BCF calculated from the K_{ow} by a food-chain multiplier (U.S. EPA, 1995a). The GLI incorporated several improvements in the methodology for deriving BAFs. For example, the GLI used the Gobas model (Gobas, 1993) for estimating FCMs that accounted for both the benthic and pelagic food webs. The Thomann model described above only accounted for the pelagic food web. Other improvements included the use of the BSAF method for estimating BAFs. The BSAF method allows for the estimation of BAFs for those chemicals that are difficult to measure in the ambient water due to their extremely high hydrophobicity, such as the polychlorinated dibenzo-p-dioxins.

The revised methodology in this Notice for deriving human health AWQC explicitly addresses various attributes of how bioaccumulative chemicals behave and accumulate in aquatic ecosystems. For certain chemicals where uptake from exposure to multiple media is important, EPA is emphasizing the assessment of bioaccumulation (i.e., uptake from water, food, sediments) over bioconcentration (i.e., uptake from water). Consistent with the final GLI, the revisions to EPA's national AWQC methodology establishes the same four-method hierarchy of procedures for deriving BAFs for nonpolar organic chemicals.

For inorganic chemicals, EPA proposes that the AWQC be based on (in order of preference): (1) an appropriately determined field-measured BAF; (2) a laboratory-measured BCF multiplied by a field-measured FCM; or (3) a laboratory-measured BCF. Because inorganic substances do not predominantly partition to lipids, the BAF for metals do not need to be normalized by lipid content.

4. Definitions

Baseline BAF (BAF_{ℓ}^{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_{ℓ}^{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:

$$BAF = \frac{C_t}{C_w} \qquad \text{(Equation IIID-3)}$$

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:

$$BCF = \frac{C_t}{C_w} \qquad \text{(Equation IIID-4)}$$

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:

$$BSAF = \frac{C_\ell}{C_{soc}} \qquad \text{(Equation IIID-5)}$$

where:

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

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

$$BMF_{(TL,\ n)} = \frac{C_{\ell\ (TL,\ n)}}{C_{\ell\ (TL,\ n-1)}} \qquad \text{(Equation IIID-6)}$$

where:

$C_{\ell\ (TL,\ n)}$ = Lipid-normalized concentration in appropriate tissue of predator organism at trophic level "n"

$C_{\ell\ (TL,\ n-1)}$ = 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:

$$BMF_{(TL,\ n)} = \frac{C_{t\ (TL,\ n)}}{C_{t\ (TL,\ n-1)}} \qquad \text{(Equation IIID-7)}$$

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:

$$C_w^{fd} = (f_{fd}) \cdot (C_w^t) \qquad \text{(Equation IIID-8)}$$

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_ℓ). 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:

$$BAF_\ell = \frac{C_\ell}{C_w} \qquad \text{(Equation IIID-9)}$$

where:

C_ℓ = Lipid-normalized concentration of the chemical in whole organism or specified tissue

C_w = Concentration of chemical in water

Lipid-normalized Bioconcentration Factor (BCF_ℓ). 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:

$$BCF_\ell = \frac{C_\ell}{C_w} \qquad \text{(Equation IIID-10)}$$

where:

C_ℓ = Lipid-normalized concentration of the chemical in whole organism or specified tissue

C_w = Concentration of chemical in water

Lipid-normalized Concentration (C_ℓ). 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:

$$C_\ell = \frac{C_t}{f_\ell} \qquad \text{(Equation IIID-11)}$$

where:

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

f_ℓ = 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:

$$C_{soc} = \frac{C_s}{f_{oc}} \qquad \text{(Equation IIID-12)}$$

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.

5. Determining Bioaccumulation Factors for Nonpolar Organic Chemicals

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 (e.g., 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 (see Section 6 for determining baseline BAFs).

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 (e.g., 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 in a baseline BAF and a BAF used in the derivation of 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 which enables extrapolation for organic chemicals from one species to another and are based on the freely dissolved concentration of organic chemicals which enables 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 baseline BAFs are those derived using appropriate field data. Field-measured BAFs, however, have not been determined for all chemicals. Thus, EPA recommends a hierarchy of procedures to determine BAF values. The data preference for derivation of baseline BAFs for nonpolar organic chemicals 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); or

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 an acceptable baseline BAF using each of the four methods is discussed in Section D.6. Section D.7 discusses the information needed to derive an acceptable BAF for use in the calculation of AWQC.

6. Estimating Baseline BAFs

All the baseline BAFs for nonpolar organic chemicals should be expressed on a freely dissolved and lipid-normalized basis. In addition, because bioaccumulation can be strongly influenced by the trophic level of aquatic organisms, baseline BAFs need to be determined on a trophic level-specific basis. The procedures for adjusting a field-measured BAF or field-measured BSAF or laboratory-measured BCF to a freely dissolved and lipid-normalized basis are discussed below.

(a) Field-Measured Baseline BAF

Appropriately derived field-measured BAFs are considered first in the data preference hierarchy for calculating baseline BAFs because they directly reflect any chemical metabolism that may occur and site-specific differences in the aquatic food web that may affect bioaccumulation. The calculation of a field-measured baseline BAF expressed on a freely dissolved and lipid-normalized basis 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 (to estimate 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:

$$\text{Baseline } BAF_{\ell}^{fd} = \left[\frac{\text{Measured } BAF_T^t}{f_{fd}} - 1 \right] \left(\frac{1}{f_{\ell}} \right) \qquad \text{(Equation IIID-13)}$$

where:

Baseline BAF_{ℓ}^{fd}	=	BAF expressed on a freely dissolved and lipid-normalized basis
Measured BAF_T^t	=	BAF based on total concentration in tissue and water
f_{ℓ}	=	Fraction of the tissue that is lipid

f_{fd} = Fraction of the total chemical that is freely dissolved in the ambient water

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:

$$\text{Measured } BAF_T^t = \frac{\text{Total concentration of chemical in tissue}}{\text{Total concentration of chemical in the ambient water}} \qquad \text{(Equation IIID-14)}$$

Application of data quality assurance procedures when measuring, estimating, and applying field-measured BAFs is of primary importance. The following general procedural and quality assurance requirements are important to be met for field-measured BAFs:

1. 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.

2. 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.

3. Collection of bioaccumulation field data at a specific site for which criteria are to be applied and with the species of concern are preferred.

4. If data cannot be collected from every site for which criteria are to be applied, 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 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 and water samples.

6. 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.

7. The concentration of the chemical in the water should be measured in a way that can be related to particulate organic carbon (POC) and/or dissolved organic carbon (DOC).

8. 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.

9. 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 is currently developing guidance for determining field-measured BAFs, including recommendations for minimum data base requirements. A more detailed discussion of the factors which need to be considered when determining field-measured BAFs is provided in the TSD.

Fraction Freely Dissolved (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, or chemicals bound to dissolved organic matter in the water. The form of the chemical has been shown to affect bioaccumulation, with the freely dissolved fraction 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, bioaccumulation factors which are based on the concentration of freely dissolved chemical in the water will provide the most universal bioaccumulation factor for organic chemicals when averaging bioaccumulation factors from different studies (i.e., BAFs based on the freely dissolved chemical are most predictable between sites). 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. Thus, if only BAFs based on total water

concentrations are reported in a given BAF study, they can be used with information on the organic carbon content of water (from the BAF study, if available) to predict freely dissolved concentrations.

To estimate the freely dissolved concentration, the fraction freely dissolved (f_{fd}) in the above equation must be estimated, using information on the chemical's K_{ow} and both dissolved and particulate organic carbon contents of the water. The equation used to estimate f_{fd} is as follows:

$$f_{fd} = \frac{1}{[1 + (POC \cdot K_{ow}) + (DOC \cdot \frac{K_{ow}}{10})]} \qquad \text{(Equation IIID-15)}$$

where:

POC = concentration of particulate organic carbon (kg/L)

DOC = concentration of dissolved organic carbon (kg/L)

K_{ow} = n-octanol water partition coefficient for the chemical

Additional information on the derivation of Equation IIID-15 is provided in the TSD.

POC/DOC Values. 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 obtained from other studies of the same site used in the BAF study or closely related site(s) within the same water body. When using POC/DOC data from other studies of the same water body, care should be taken to ensure that environmental conditions that may affect POC or DOC

concentrations are reasonably similar to those in the BAF study. Additional guidance on selection of POC and DOC values is provided in the TSD.

K_{ow} Values. The K_{ow} is the octanol-water partition coefficient of a chemical and is defined as the ratio of the concentration of a substance in the n-octanol phase to its concentration in the aqueous phase. Numerous investigations 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. Isnard and Lambert (1988) list various regression equations that illustrate this linear relationship. The underlying assumption for the linear relationship between the BCF and K_{ow} is that the bioconcentration process can be viewed as a partitioning of a chemical between the lipid of the aquatic organisms and water and that the K_{ow} is an useful surrogate for this partitioning process (Mackay, 1982).

Several of the BAF procedures, including the BSAF method, use of the food chain model, and conversion of total chemical concentrations in water to freely dissolved chemical concentrations, rely on the K_{ow} for chemicals. Because the K_{ow} is used in calculating BAFs, it is important that the most accurate and reliable K_{ow} measurements for a chemical are used. 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.

In this Notice, EPA discusses 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 undergoing external peer review. The salient features of both the GLWQI K_{ow} selection guidance (option one) and EPA's new, draft guidance (option two) are presented below. Additional details of both approaches are provided in the TSD.

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 $K_{ow} \geq 4$:

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, then 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 K_{ow} value is available for a chemical using the highest priority method, then 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 nonradioactive techniques. The values determined using radioactive methods should be moved down one step in the priority below the values determined using the nonradioactive technique. 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} is > 8,

A. Develop independent estimates of K_{ow} using:

1. Liquid Chromatography (LC) methods with "appropriate" standards. (See TSD 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 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 the TSD.

C. If calculated/estimated data do not agree, use professional judgement to evaluate/blend/weight the calculated and estimated data to assign K_{ow} value.

D. Document rationale including relevant statistics.

III. If calculated log K_{ow} ranges 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} is < 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 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 ≤ log K_{ow} ≤ 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 for measuring or calculating K_{ow} that are referenced in both approaches above 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).

- 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.

- 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 their chemical structure with measured K_{ow} values. The method used to calculate the K_{ow} values is described in Hansch and Leo (1979).

- **LOGKOW** is essentially an expanded CLOGP with more recent training data and additional fragment constants. The developers were Philip Howard, William Meylan and co-workers at Syracuse Research Corporation. (See Meylan and Howard, 1994, for model details and performance information.)

- **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 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 total BAF to a composite baseline BAF, a composite K_{ow} value for the mixture can be calculated based on the sum of the total concentrations of the mixture components in water (e.g., individual congeners for PCBs), the sum of the dissolved concentrations of the mixture components in water, and the DOC and POC from the site for which the BAF was measured. An example of determining a composite K_{ow} for deriving BAFs and AWQC for PCBs under the Great Lakes Water Quality Initiative is provided in 62 FR 117250 (March 12, 1997). Additional details on this methodology are also provided in the TSD.

Fraction lipid (f_l) - lipid normalization of data. For lipophilic nonpolar organic chemicals, BAFs and BCFs are assumed to be directly proportional to the percent lipid in the edible tissue or whole body of the organism of interest. For example, an organism with two percent lipid content would be expected to accumulate twice the amount of a chemical as an organism with one percent lipid content, all else being equal. The proportionality of accumulation with lipid content for nonpolar organic chemicals has been extensively evaluated in the literature (Mackay, 1982; Connell, 1988; Barron, 1990) and is generally accepted. Different aquatic organisms, however, have different lipid contents thus making it difficult to compare BAFs and BCFs. BAFs and BCFs that have been measured in aquatic organisms that have different lipid contents can be compared by normalizing the lipids between organisms. The lipid values can be normalized by dividing the BAF or BCF by the mean lipid fraction in the tissue of the aquatic organism sampled. For example, if the BAF for

a given chemical and tissue of an aquatic organism was determined to be 5,000 L/kg and the percent lipid in this tissue was 5 percent, the lipid-normalized BAF would be 100,000 L/kg-lipid (i.e., 5,000/0.05).

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 in the test organism.

(b) Baseline BAF Derived from BSAFs

When acceptable field-measured values of the BAF are not available for a nonpolar organic chemical, EPA recommends the use of the BSAF methodology to predict the BAF as the second method 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 may also be used to estimate BAFs (USEPA, 1993), as described below. Since 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 which are detectable in fish tissues and sediments, but are difficult to measure in the water column and have reduced bioaccumulation potential due to metabolism.

In previously promulgated guidance, ratios of BSAFs of polychlorinated dibenzodioxins and polychlorinated dibenzofurans to a BSAF for 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) were used for evaluation of TCDD toxic equivalency associated with complex mixtures of these chemicals (i.e., bioaccumulation equivalency factors, see 60 FR 15366). This approach is applicable to calculation of BAFs from BSAFs for other organic chemicals. The approach of estimating BAFs from BSAFs requires data from a steady-state (or near steady-state condition) between sediment and water for both a reference chemical "r" with a measured BAF and other chemicals "n=i" for which BAFs are to be determined. The baseline BAF derived from a BSAF for a chemical "i" can be calculated using the following equation:

$$(\text{Baseline } BAF_{\ell}^{fd})_i = (\text{Baseline } BAF_{\ell}^{fd})_r \cdot \left(\frac{(BSAF)_i \cdot (K_{ow})_i}{(BSAF)_r \cdot (K_{ow})_r} \right) \qquad \text{(Equation IIID-16)}$$

where:

$(\text{Baseline } BAF_{\ell}^{fd})_i$ = BAF expressed on a freely dissolved and lipid-normalized basis for chemical of interest "i"

$(\text{Baseline } BAF_{\ell}^{fd})_r$ = BAF expressed on a freely dissolved and lipid-normalized basis for reference chemical "r"

$(BSAF)_i$ = Biota-sediment accumulation factor for chemical of interest "i"

$(BSAF)_r$ = Biota-sediment accumulation factor for the reference chemical "r"

$(K_{ow})_i$ = octanol-water partition coefficient for chemical of interest "i"

$(K_{ow})_r$ = octanol-water partition coefficient for the reference chemical "r"

Field-measured BSAFs. As shown in the following equation, BSAFs are determined by relating lipid-normalized concentrations of chemicals in an organism (C_ℓ) to organic carbon-normalized concentrations of the chemicals in surface sediment samples associated with the average exposure environment of the organism (C_{soc}).

$$BSAF = \frac{C_\ell}{C_{soc}} \qquad \text{(Equation IIID-17)}$$

The lipid-normalized concentration of a chemical in an organism is determined by:

$$C_\ell = \frac{C_t}{f_\ell} \qquad \text{(Equation IIID-18)}$$

where:

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

f_ℓ = Fraction lipid content in the organism

The organic carbon-normalized concentration of a chemical in sediment is determined by:

$$C_{soc} = \frac{C_s}{f_{oc}} \qquad \text{(Equation IIID-19)}$$

where:

C_s = Concentration of chemical in sediment (μg/g sediment)

f_{oc} = Fraction organic carbon in sediment

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 (i.e., the ratio of the freely dissolved concentration associated with water in the tissue to the freely dissolved concentration associated with the pore water in the sediment). At equilibrium, the disequilibrium (fugacity) ratio between biota and sediment is expected to be 1.0. However, deviations from 1.0 (reflecting disequilibrium) are common and can reflect biomagnification, conditions where surface sediment has not reached equilibrium, kinetic limitations for chemical transfer, or biological processes such as growth or biotransformation. BSAFs are most useful (i.e., most predictable from one site to another) 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.

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.

The following procedural and quality assurance requirements should be met for field-measured BSAFs:

1. 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.

2. 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.

3. The K_{ow}s used should be of acceptable quality as described in Section D.6 above.

4. 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 apply.

5. The percent lipid should be either measured or reliably estimated for the tissue used in the determination of the BAF.

Further details on these requirements for predicting BAFs from BSAF measurements and the data supporting this approach are provided in the TSD.

(c) Calculation of a Baseline BAF from a Laboratory-Measured BCF and FCM

As 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 FCM. Laboratory-measured BCFs are preferred over predicted BCFs because laboratory-measured BCFs inherently account for the effects of any metabolism of the chemical on the BCF. The equation for deriving a baseline BAF expressed on a freely dissolved and lipid-normalized basis using this method is:

$$\text{Baseline } BAF_{\ell}^{fd} = (FCM) \cdot \left[\frac{\text{Measured } BCF_T^t}{f_{fd}} - 1 \right] \cdot \left(\frac{1}{f_{\ell}} \right) \qquad \text{(Equation IIID-20)}$$

where:

Baseline BAF_{ℓ}^{fd}	=	BAF expressed on a freely dissolved and lipid-normalized basis for a given trophic level
Measured BCF_T^t	=	BCF based on total concentration in tissue and water
f_{ℓ}	=	Fraction of the tissue that is lipid

f_{fd}	=	Fraction of the total chemical in the test water that is freely dissolved
FCM	=	The food-chain multiplier either obtained from Tables IIID-1, IIID-2, or IIID-3 by linear interpolation for the appropriate trophic level, 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.

Measured BCF_T^t. To estimate a measured BCF_T^t, information is needed on the total concentration of the chemical in the tissue of the organism and the total concentration of the chemical in the laboratory test waters. The equation to derive a measured BCF_T^t is:

$$\text{Measured } BCF_T^t = \frac{\text{Total concentration of chemical in tissue}}{\text{Total concentration of chemical in test water}} \qquad \text{(Equation IIID-21)}$$

A 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 for such a

chemical 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 that is above concentrations existing in the control water 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, which can be particularly important in affecting BCF determinations for poorly depurated chemicals.

11. Other aspects of the methodology used should be similar to those described by the American Society of Testing and Materials (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 obtain steady state conditions between the organism and the water column.

FCMs. The FCM reflects a chemical's tendency to biomagnify in the aquatic food web. Food chain multipliers in Tables IIID-1, IIID-2 and IIID-3 have been calculated as the ratio of the baseline BAFs for various trophic levels to the baseline BCF using the model of Gobas (1993). Values of FCMs greater than 1.0 indicate biomagnification and typically apply to organic chemicals with log K_{ow} values between 4.0 and 9.0. For a given chemical, FCMs tend to be greater at higher trophic levels, although FCMs for trophic level three can be higher than those for trophic level four. The final GLI established FCMs using the food chain model by Gobas (1993) for a range of log K_{ow} values from 2.0 to 9.0 at intervals of a tenth of a log K_{ow} value.

EPA recommends using the biomagnification model by Gobas (1993) to derive FCMs for nonpolar organic chemicals for several reasons. First, the Gobas model includes both benthic and pelagic food chains, thereby 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 predicted BAFs using the model 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 model requires input of specific data on the structure of the food chain and the water quality characteristics of the water body of interest. For example, in the GLI and in these proposed revisions to the AWQC methodology, it is assumed that the food chain consists of four trophic levels. Trophic level 1 is phytoplankton, trophic level 2 is zooplankton, trophic level 3 is forage fish (e.g., sculpin and smelt), and trophic level 4 are predator fish (e.g., salmonids). Additional assumptions must be made regarding the composition of the aquatic species diet (e.g., salmonids consume 10 percent sculpin, 50 percent alewives, and 40 percent smelt), the physical parameters of the aquatic species (e.g., lipid values), and the water quality characteristics (e.g., water temperature, sediment organic carbon).

EPA has estimated FCMs using three different potential food web structures. The first food web structure includes both a benthic and pelagic food chains. The FCMs range from 1.00 to about 27 for log K_{ow} values ranging from 2.0 to 9.0. The second food web structure includes only the pelagic food chain. The FCMs for this food web structure range from 1.0 to about 4 for log K_{ow} values ranging from 2.0 to 9.0. Finally, the third food web structure includes only the benthic food chain. The FCMs for this scenario range from 1.0 to about 57 for log K_{ow} values ranging from 2.0 to 9.0. The resulting FCMs for trophic levels 2, 3, and 4 are included in Tables IIID-1, IIID-2, and

IIID-3. A more detailed discussion on the model and the input parameters for the model are included in the TSD for BAFs.

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 chemicals because appropriate model-derived estimates are not yet available (see Section D.8). Similarly, field-measured FCMs can also be determined for organic chemicals. 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 derivation of a BAF.

Table IIID-1

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

Table IIID-1

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
6.7	1.000	14.223	26.363
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 IIID-2

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

Table IIID-2

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
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
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.

Table IIID-3

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

Table IIID-3

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
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
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

- The FCMs for trophic level 3 are the geometric mean of the FCMs for sculpin and alewife.

As discussed below and in the TSD, FCMs are related to and can be determined from biomagnification factors (BMF). For example:

$$FCM_{TL2} = BMF_{TL2} \quad \text{(Equation IIID-22)}$$

$$FCM_{TL3} = (BMF_{TL3})\,(BMF_{TL2}) \quad \text{(Equation IIID-23)}$$

$$FCM_{TL4} = (BMF_{TL4})\,(BMF_{TL3})\,(BMF_{TL2}) \quad \text{(Equation IIID-24)}$$

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 tissue residue concentrations determined in biota at a site according to the following equation.

$$BMF_{TL2} = (C_{\ell,TL2}) / (C_{\ell,TL1}) \quad \text{(Equation IIID-25)}$$

$$BMF_{TL3} = (C_{\ell,TL3}) / (C_{\ell,TL2}) \quad \text{(Equation IIID-26)}$$

$$BMF_{TL4} = (C_{\ell,TL4}) / (C_{\ell,TL3}) \quad \text{(Equation IIID-27)}$$

where:

C_t = 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 (U.S. EPA, 1995b; 1995c, 1995d) 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 over the time period required to achieve steady-state conditions for the contaminant in the target species.

(d) Calculation of a Baseline BAF from a K_{ow} and FCM

As the fourth tier in the data preference hierarchy for nonpolar organic chemicals (e.g., when acceptable, field-measured BAFs, BSAFs, or laboratory-measured BCFs are unavailable), EPA recommends the use of the K_{ow} for a chemical and a FCM for estimating baseline BAFs at various trophic levels. For each trophic level, a predicted baseline BAF can be calculated as:

$$\text{Baseline } BAF_{\ell}^{fd} = (FCM) \cdot (K_{ow}) \qquad \text{(Equation IIID-28)}$$

where:

Baseline BAF_{ℓ}^{fd} =		BAF expressed on a freely dissolved and lipid-normalized basis for a given trophic level
FCM	=	The food-chain multiplier obtained from tables IIID-1 to IIID-3 by linear interpolation (or from appropriate field data) for the appropriate trophic level
K_{ow}	=	Octanol-water partition coefficient

This equation is based on the assumption that a baseline BCF is approximately equal to the K_{ow} for the chemical. This equation was used in the final GLI and its derivation is included in the TSD.

(e) Metabolism

Many organic chemicals that are accumulated 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. Field-measured BAFs and BSAFs automatically take into account any metabolism that occurs and therefore more accurately predict bioaccumulation than predicted BAFs based on laboratory measurements. Because of the uncertainties associated with predicting chemical metabolism, EPA prefers that the bioaccumulation potential of a chemical be determined based on field data. Predicted BAFs obtained by multiplying laboratory-measured BCFs by a field-measured FCM also take into account chemical metabolism if it occurs. 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 do not take into account the effect of metabolism on the FCM. Predicted BAFs that are obtained by multiplying a predicted BCF by a FCM make no allowance for metabolism.

EPA is aware that for some chemical classes, such as PAHs, metabolism can have a significant effect on the bioaccumulation for the chemical. Unfortunately, EPA is not aware of any generalized approach for predicting the effects of metabolism. For this reason, EPA suggests that BAFs be reviewed for consistency with all available data concerning bioaccumulation of a chemical. In particular, information on metabolism, molecular size, or other physicochemical properties which might enhance or inhibit bioaccumulation should be considered.

7. BAFs Used in Deriving AWQC

After the baseline BAF has been derived for a nonpolar organic chemical using one of the four methods described above, 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. For each trophic level, the equation for calculating a BAF for use in deriving the AWQC is:

$$\text{BAF for AWQC}_{(TL\ n)} = [(\text{Baseline BAF}_{\ell}^{fd})_{TL\ n} \cdot (f_{\ell})_{TL\ n} + 1] \cdot (f_{fd}) \qquad \text{(Equation IIID-29)}$$

where:

Baseline BAF_{ℓ}^{fd}	=	BAF expressed on a freely dissolved and lipid-normalized basis for trophic level "n"
$f_{\ell(TL\ n)}$	=	Fraction lipid of aquatic species consumed at trophic level "n"
f_{fd}	=	Fraction of the total chemical in water that is freely dissolved

Baseline BAF. The baseline BAFs used in this equation are those derived from the equations presented in Section D.6 above.

Lipid Content of Aquatic Species Consumed by Humans. As discussed above, the percent lipid of the aquatic species consumed by humans is needed when deriving BAFs for a chemical that will be used for deriving AWQC. This information is needed to provide an accurate characterization of

the potential exposure to a chemical from ingestion of aquatic organisms. The percent lipid fraction used when calculating a BAF should, if possible, be weighted by the consumption rate of those aquatic species consumed by the target population (e.g., general population, sport anglers, subsistence fishers). A consumption-weighted percent lipid is recommended because it provides a more accurate characterization of the potential exposure to humans than simply averaging lipid values from a variety of species in a given geographic area which may or may not be eaten by humans. 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. For each trophic level, the consumption-weighted fraction lipid can be determined by the following equation:

$$f_\ell = \sum \left[\frac{CR_i}{CR_{tot}} \bullet f_{\ell,i} \right] \qquad \text{(Equation IIID-30)}$$

where:

f_ℓ = Lipid fraction representative of aquatic species at a given trophic level eaten by the target population

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

$f_{\ell,i}$ = Lipid fraction of species "i" eaten by the target population

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 value that combines data across relevant trophic levels.

To estimate the consumption-weighted percent lipid content of consumed aquatic species within various trophic levels, information is needed on: (1) the type and quantity of aquatic biota consumed by humans, (2) the trophic position of those species, and (3) the percent lipid of the aquatic biota consumed by humans. The types and quantity of aquatic species eaten by individuals differ throughout the United States. Thus, to determine the lipid content of the aquatic species of interest (e.g., freshwater and estuarine finfish and shellfish) eaten by local populations, EPA recommends that States use available local information on consumption rates specific to the types and quantity of aquatic species eaten by target populations. Data on consumption rates of species may be available from fish and shellfish consumption surveys conducted within the State or in States or regions that have similar finfish and shellfish species. EPA has published the document *Consumption Surveys for Fish and Shellfish. A Review and Analysis of Survey Methods* (Feb. 1992, EPA 822/R-92-001) which may assist in conducting and analyzing the results of such surveys. If local data on species-specific consumption rates are not available, States may wish to use regional data on consumption rates of aquatic species found in fresh and estuarine waters, available from USDA's CSFII (USEPA, 1998). These regional data from the CSFII are presented in the TSD accompanying this Notice. Such data may be used with local data on lipid contents of the consumed aquatic species.

The second type of information required is data on the trophic level of consumed aquatic species corresponding to the consumption rate survey. In order to estimate trophic position, information on the dietary preferences of the organisms of interest is required. The dietary composition (and trophic level) of aquatic organisms can vary with the size and age of the organism, the type of ecosystem, season, and other factors, which can complicate precise determinations of trophic level status. Therefore, whenever possible, it is recommended that information on such attributes (particularly size of consumed organisms) be obtained from the consumption survey. EPA has developed draft guidance on estimating trophic status of numerous aquatic species, in addition to the wildlife that consume them, which is currently being finalized (USEPA 1995b; 1995c; 1995d). Once finalized, this guidance is recommended in situations where sufficient local information on trophic status is not available.

The third critical piece of information is the percent lipid values of the aquatic biota consumed by humans. The lipid content of a particular aquatic species may vary by geographic region, possibly a result of different dietary composition. Therefore, lipid values based on good-quality data from species consumed by the local population of interest are more appropriate than nationally derived values. 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 IIID-30 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 (rounded to two significant digits for convenience).

It should be noted that if a national default lipid value was determined based only on the species with the **highest** mean lipid content within each CSFII species category and trophic level (e.g., giving 100 percent of the weighting to lake trout which has the highest lipid content among the species in the trout category), the resulting consumption-weighted lipid values are 3.0% at trophic level 2, 2.2% at trophic level 3, and 6.2% at trophic level 4. The reason that there is not greater difference between the mean and high estimates of the default lipid values within each trophic level is probably due to the fact that the national mean consumption rates in the CSFII survey are weighted heavily by relatively lean aquatic organisms such as shrimp, crab, perch, and flounder. Because local or regional consumption patterns may deviate from national norms, it is further recommended that local and regional data on consumption patterns be used whenever available. When such local consumption data are used, however, information on lipid content of those locally-consumed species is also required (national default consumption-weighted lipid content values do not necessarily apply to local consumption data). Additional description of the data and methods to derive the default lipid values are provided in the TSD accompanying this Notice.

Freely Dissolved Fraction. Equation IIID-15 for estimating the fraction freely dissolved for baseline BAFs is also used here. In this case, however, the POC and DOC values should be based on the site where the BAF and the criterion will be applied and not where the samples were collected. If the POC and DOC values are not available for that site, then data from sites expected to be similar to those to which the AWQC is being applied can be used. 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 50th 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. Based on these data, EPA has also derived default values at a more disaggregated level (e.g., for individual States and water body types) which, in some situations, may provide more appropriate estimates of POC and DOC concentrations associated with the field BAF study than the national default medians listed above. Additional description of the STORET DOC/POC data base used to derive the default values, including POC and DOC information presented at a more disaggregated level, is provided in the TSD. The K_{ow} value for the chemical will be the same as used for deriving the baseline BAF for the chemical.

As noted above, standardizing BAFs based on the freely dissolved concentration in water allows a common basis for averaging BAFs from several studies. However, for use in criteria development, these BAFs must be converted back to values based on the total concentration in the water to be consistent with monitored water column and effluent concentrations, which are typically based on total concentrations of chemicals in the water. This is done simply by multiplying the freely dissolved baseline BAF by the fraction of the freely dissolved chemical in water bodies where criteria are to be set, as shown in Equation IIID-29.

8. Inorganic Substances

For inorganic chemicals, either (1) a field-measured BAF; (2) a laboratory-measured BCF multiplied by a field-measured FCM; or (3) a laboratory-measured BCF should be used. These measured values are recommended because no method is available for reliably predicting BCFs or

BAFs for inorganic chemicals; BCFs and BAFs vary from one invertebrate to another, from one fish to another, and from one tissue to another. Unlike nonpolar organic chemicals, lipid normalization does not apply. For many inorganic chemicals, the BCF will be equal to the BAF. In other words, for these chemicals there is no measurable bioaccumulation from food or other nonwater sources. There are exceptions however, such as mercury and selenium, which can bioaccumulate substantially.

9. SAB Comments

EPA's Science Advisory Board has reviewed the BAF methodology three times since 1992. In December of 1992, SAB issued the report "Evaluation of the Guidance for the Great Lakes Water Quality Initiative"(EPA-SAB-EPEC/DWC-93-005). The SAB reviewed four technical guidance documents for developing water quality criteria in the Great Lakes Basin as a part of the Proposed Great Lakes Water Quality Initiative including the proposed GLI BAF methodology. The 1992 SAB report stated that:

The subcommittee finds the BAF procedure is more advanced and scientifically credible than existing BCF procedures. The use of the BCF, FCM, and BAF approach appear to be fundamentally sound. However, a major inconsistency exists between field data for some chemicals (Reinert, 1970) and the conceptual model of Thomann (1989) for food chain derived residues. Efforts should be devoted to clarifying and improving the documentation and the issues discussed below with a view to presenting a straight-forward procedure with associated estimates of confidence levels. It is the Subcommittee's opinion that with some modification a credible BAF estimation method can be

developed exploiting present knowledge. Based on the SAB comments, EPA revised the BAF methodology and finalized the GLI in March 1995.

The second SAB review occurred as part of the overall review of the Revisions to the AWQC methodology. The SAB provided a report called "Review of the Ongoing Revisions of the Methodology for Deriving National Ambient Water Quality Criteria for the Protection of Human Health" which stated:

> We strongly urge the Agency to base AWQC on sound experimental evidence that bioaccumulation does occur, rather than on hypothetical assumptions that bioaccumulation might occur. The Committee believes that the strategy of setting AWQC by measuring contaminant concentrations in certain biota and then applying either a BCF or a BAF to calculate water concentrations may not accurately reflect the complex ways in which the real environment operates. Although we support EPA's efforts to develop well-validated BAFs, for the time being the Committee recommends that the Agency rely more heavily on BCFs rather than BAFs, because of the higher likelihood of collecting an adequate BCF data base.

Finally, in September 1995, the SAB provided a report to EPA entitled "Commentary on Bioaccumulation Modeling Issues" (SAB-EPEC/DWC-COM-95-006). The report was the result of a April 1994 consultation with the SAB on approaches for estimating bioaccumulation potential of chemicals and to discuss various mass/balance/food web models. The SAB provided general

advice on how and when EPA should use mass balance/food web models to estimate bioaccumulation and what research is needed to improve model predictions. The SAB stated:

> In summary, while the Subcommittee agrees that mass balance/food web models such as the Thomann model hold promise for predicting bioaccumulation of certain types of chemicals, we urge the Agency to further field test the models for additional classes of compounds and for additional environmental settings and assess the uncertainties in model prediction prior to their wide-spread application in a regulatory context. Ongoing peer review should be an integral part of this process. Finally, the use of models, no matter how refined, should be augmented by appropriately designed laboratory and field experiments and monitoring.

After careful consideration and review of the SAB's comments, EPA recommends using BAFs in the derivation of AWQC because, for highly lipophilic chemicals, uptake from aquatic organisms is the primary route of exposure. Failing to account for all routes of exposure, including ambient water and diet, would result in criteria which are under protective for a substantial portion of the population. In addition, the data hierarchy proposed above relies upon using the most scientifically sound experimental evidence of bioaccumulation. Specifically, the first and second preference for deriving BAFs for organic chemicals relies on using properly collected and analyzed field data over predicted bioaccumulation factors based on models. However, in the absence of field data for a chemical, EPA believes the use of bioaccumulation models can be used in establishing the regulatory criteria when the models have been properly validated. Using data from the Great Lakes,

EPA has evaluated the predictability of BAFs determined from the Gobas model (and those determined from BSAFs). EPA found measured and predicted BAFs to be generally in good agreement when field-measured BAFs are adjusted to account for the lipid and freely dissolved fractions. Additional information on these comparisons is provided in the TSD.

10. Issues for Public Comment

Comments are requested on the following issues in the proposal:

1. Is the suggested hierarchy for developing BAFs appropriate? Are there any alternatives to the four methods that could be used to derive AWQC?

2. Is the procedure for estimating the consumption-weighted default lipid value of 2 percent for aquatic species eaten by humans and the data used for deriving the value appropriate? Are there other data available that could be used to calculate the default lipid value?

3. Are there alternatives to the equation used to derive the freely dissolved fraction of a chemical appropriate? If yes, what data support an alternative approach? Are there scientifically defensible alternatives to EPA's K_{ow}-based estimate of K_{DOC} and K_{POC}?

4. Are the default POC value of 0.48 mg/L and the default DOC value of 2.9 mg/L used in deriving BAFs appropriate as national defaults? Are the water body- and State-specific POC and

DOC values provided in the TSD appropriate? Are there additional data that could be used to derive these values?

5. What approaches could be used to account for metabolism in the determination of a BAF and what data are available to support these approaches?

6. What other models are available that could be used to predict FCMs? What are the data that support these models? Is EPA's choice of food web structures used to calculate FCMs appropriate?

7. Is EPA's guidance on selecting reproducible K_{ow} values appropriate? Which of the two options for selecting reproducible K_{ow} values do you consider most appropriate?

8. Should properly derived field-measured FCMs take precedence over FCMs derived using the Gobas (1993) model?

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E. Microbiology

1. Existing Microbiological Criteria

The 1980 AWQC National Methodology did not address microbiological criteria for the protection of human health. However, in 1986 EPA published a document entitled Bacteriological Ambient Water Quality Criteria for Marine and Fresh Recreational Water, which updated and revised bacteriological criteria previously published in 1976 in Quality Criteria for Water.

The microbiological criteria developed in 1986 are based on research conducted on beaches that were officially designated for swimming and had well-defined sources of human fecal pollution. Researchers examined the relationship between swimming-associated gastrointestinal (GI) illness

and ambient densities of indicator bacteria. EPA concluded from these studies that measuring the densities of the indicator organism group recommended in the 1976 criteria, the fecal coliform, is inadequate. The enumeration of the recommended indicators is based on analytical procedures described in USEPA (1976). The EPA studies demonstrated that *enterococci* densities correlate far better with swimming illness in both marine and fresh water than fecal coliform densities. Also, *E.coli*, a specific bacterial species included in the fecal coliform group, correlates as well as *enterococci* with GI illness in fresh water but does not correlate as well in marine water.

The recommended densities of indicator organisms (*E.coli* and *enterococci*), upon which the 1986 criteria are based, were calculated to approximate the degree of protection already accepted using fecal coliforms as indicators. The current EPA criteria are as follows:

Fresh water: *E. coli* not to exceed 126/100 ml or *enterococci* not to exceed 33/100 ml;

Marine water: *enterococci* not to exceed 35/100 ml.

These criteria are calculated as the geometric mean of a statistically sufficient number of samples, generally no fewer than five, equally spaced over a 30-day period.

No single sample should exceed a one-sided confidence limit (C.L.) calculated using the following as guidance:

Designated bathing beach:	75% C.L.
Moderate use for bathing:	82% C.L.
Light use for bathing:	90% C.L.
Infrequent use for bathing:	95% C.L.

These confidence limits are based on a site-specific log standard deviation or, if site data are not sufficient to establish a log standard deviation, then using 0.4 as the log standard deviation for both indicators in fresh water. In marine water one would use 0.7 as the log standard deviation.

The quantitative relationship between the rates of swimming-associated health effects (acute GI infection) and bacterial indicator densities was determined using regression analysis. Linear relationships were estimated from data grouped on the basis of summers or trials with similar indicator densities. The data for each summer were analyzed by pairing the geometric mean indicator density for a summer bathing season at each beach with the corresponding swimming-associated GI illness rate for the same summer. The swimming-associated illness rate was determined by subtracting the GI illness rate in non swimmers from that in swimmers. These two variables from multiple beach sites were used to calculate a regression coefficient, y-intercept, and 95 percent confidence intervals for the paired data. In the marine studies, the total number of points for use in regression analysis was increased by collecting trial days with similar indicator densities from each study location and placing them into groups. The swimming-associated illness rate was determined as above, by subtracting non swimmers' illness rate of all the individuals included in the grouped trial days from the swimmers' illness rate during these same grouped trial days.

2. Plans for Future Work

EPA recommends no change at this time in the stringency of its bacterial criteria for recreational waters; existing criteria and methodologies from 1986 will still apply. The Agency plans to conduct national studies on improving indicators together with epidemiology studies for new criteria development.

EPA will consider revising the criteria with the possible inclusion of criteria for other primary-contact waters with reduced swimming or full-body-contact use. The Agency will perform critical evaluation of studies of the health effects of recreational water microbiology. EPA will also form a group of experts from EPA program offices, ORD, and the regions to initiate development of consensus recommendations on the development of policy and criteria methodology, research and implementation strategy for a comprehensive recreational waters program.

The Agency expects to make final recommendation for action as soon as possible. A separate *Federal Register* proposal with revised criteria and methodology is anticipated for publication after improved indicator methods and associated exposure risks are established. In 1997, EPA will approve a new 24-hour enterococcus test for recreational waters that may be used as an alternative to the 48-hour test.

3. SAB Comments

(a) The SAB believes that it would be highly beneficial to establish and implement a multi-organizational working group made up of representatives from EPA, CDC, FDA, academia, the water and wastewater industry, and the public.

(b) The SAB believes that despite the desirability of and need for a comprehensive and integrated approach to ambient water quality, it is unrealistic, perhaps inappropriate, and in all likelihood impossible to address all of the water-related exposure routes of microbial health effects concerns under this regulatory initiative.

(c) The SAB recommends that the process of developing and evaluating water quality criteria for microbes should include microbes causing fecally transmitted diseases other than gastroenteritis. Such a process should also include microbes causing diseases of the skin, respiratory tract, eye, ear, nose, throat, and perhaps other sites of entry and infection.

(d) The current recreational-water quality criteria are neither appropriate for nor transferrable to other ambient waters. These criteria were intended to address only those pathogens causing enteric (GI) illness.

(e) The SAB recommends that the likelihood of human exposure to different types of ambient water be the basis for identifying the types of ambient waters for which criteria need to be

developed. The need for quality criteria for recreational waters has been established; however, the need for such criteria for some other waters has not been established.

(f) The SAB believes that a risk-based approach to criteria for pathogenic microorganisms in ambient waters is both appropriate and feasible for at least some pathogens. However, the SAB believes that this approach has limited applicability to the quality criteria for microbial pathogens in ambient waters.

(g) The SAB believes that further research has to be done on identifying, characterizing, and measuring the virulence determinants of microbial pathogens; on the factors governing or influencing the expression of these determinants under different environmental conditions; and on the role of other factors in virulence expression, such as host factors.

(h) The SAB believes that the currently approved indicator organisms in beach waters are probably appropriate for the safety of bathing waters against GI disease. The SAB believes that the currently accepted levels of the bacterial indicators are not uniformly and adequately protective of health risks from non-GI pathogens in bathing waters.

(i) The SAB believes that there are candidate alternative indicators worthy of consideration and deserving of investigation for improving ambient-water monitoring.

The EPA Office of Water agrees with the SAB comments for all the above points. The Agency makes the following recommendations:

- Future criteria development should consider the risk of diseases other than gastroenteritis. The nature and significance of other than the classical waterborne pathogens are to some degree tied to the particular type of ambient water.

- EPA needs to consider and evaluate such water-related exposure routes as inhalation and dermal absorption when addressing microbial health effects.

- A new set of indicator organisms may need to be developed for tropical water if it is proven that the current fecal indicators can grow in pristine waters or on plants in the tropics. Some potential alternative indicators to be fully explored are coliphage, other bacteriophage, and *Clostridium perfringens*.

- Because animal sources of pathogens of concern for human infection such as *Giardia*, *Cryptosporidium*, and *Salmonella* may be waterborne or washed into water and thus become a potential source for infection, they must not be ignored in risk assessment. One possible approach to estimating levels of pathogens from animal sources is to determine the ratios of conventional indicators from human sources and from animal sources. Alternatively, new indicators could be developed that are specific to or can discriminate animal sources. The presence of such indicator pathogens together with a predominance of indicators of animal wastes would help define types of risks.

- EPA needs to develop additional data on secondary infection routes and infection rates from prospective epidemiology studies and outbreaks.

- EPA needs to improve sampling, strategies for recreational water monitoring including consideration of rain fall and pollution events to trigger sampling.

References for Microbiology

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F. Other Considerations

1. Minimum Data Considerations

For many of the preceding technical areas, considerations have been presented for data quality in developing toxicological and exposure assessments. For greater detail and discussion of minimum data recommendations, the reader is referred to the TSD which accompanies this *Federal Register* Notice.

2. 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 Notice, 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. 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 EPA to 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.

In today's Notice, EPA is not recommending a methodology for developing organoleptic criteria, but rather is asking for comment on the following questions: 1. How would organoleptic criteria be used if the Agency were to develop new criteria? (Could they be used in a similar fashion to the secondary standards developed by the Agency's National Drinking Water program?) 2. Would organoleptic criteria ultimately be counterproductive if they are much lower than toxicity-based criteria?

4. 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 there were insufficient data 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 provides 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 provides 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.

Today's Notice 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 is great (such as in the case of chlorinated dioxins and furans), toxicity equivalency factors (TEFs) may be more appropriately developed than one class criterion. The Agency requests comments on the practice of developing criteria for classes of compounds and whether the guidance provided here is sufficient to ensure that class criteria are derived appropriately.

5. 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 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 today's Notice, 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.

Appendix IV. Summary of Ambient Water Quality Criteria for the Protection of Human Health: Acrylonitrile[16]

This criteria document updates the national criteria for acrylonitrile using new methods and information described in this Federal Register Notice and Technical Support Document (USEPA, 1998a) 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, 1998b).

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.

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[16] 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.

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 1998b). 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 (1998a). 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

$$AWQC = RSD \times \left(\frac{BW}{DI + \sum_{i=2}^{4} (FI_i \times BAF_i)} \right)$$

The cancer-based AWQC was calculated using the RSD and other input parameters listed below:

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 x 10^{-5} mg/L (or 0.05 µg/L), for a 10^{-6} (one in a million) lifetime cancer risk.

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, 1998a).

References

USEPA. 1998a. Ambient Water Quality Criteria Derivation Methodology–Human Health. Technical Support Document. Final Draft. EPA 822-B-98-005. Office of Water. Washington, DC. July.

USEPA. 1998b. Ambient Water Quality Criteria for the Protection of Human Health: Acrylonitrile. EPA 822-R-98-006.

Appendix V. Summary of Ambient Water Quality Criteria for the Protection of Human Health: 1,3-Dichloropropene[17]

This criteria document updates the national criteria for 1,3-DCP using new methods and information described in this *Federal Register* Notice and Technical Support Document (USEPA, 1998a) 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, 1998b).

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 EPA's 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

[17] 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.

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, 1998b).

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 this *Federal Register* Notice and in the Technical Support Document (USEPA, 1998a). 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 1.0×10^{-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 3.4×10^{-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.

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, 1998a).

References

USEPA. 1998a. Ambient Water Quality Criteria Derivation Methodology–Human Health. Technical Support Document. Final Draft. EPA 822-B-98-005. Office of Water. Washington, DC. July.

USEPA. 1998b. Ambient Water Quality Criteria for the Protection of Human Health: 1,3-Dichloropropene (1,3-DCP). EPA 822-R-98-005.

Appendix VI. Summary of Ambient Water Quality Criteria for the Protection of Human Health: Hexachlorobutadiene[18]

This criteria document updates the national criteria for HCBD using new methods and information described in this *Federal Register* Notice and Technical Support Document (USEPA, 1998a) 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, 1998b).

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, ground

[18] 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.

water and surface waters across the U.S. (see USEPA 1998b for a summary). The vast majority of samples are at trace levels or below the detection limits (DL ≈ 0.1 mg/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 this *Federal Register* Notice and in the Technical Support Document (USEPA, 1998a). 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.

$$AWQC = \left(\frac{Pdp}{SF} - RSC\right) \times \left(\frac{BW}{DI + \sum_{i=2}^{4}(FI_i \times BAF_i)}\right)$$

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, 1998a).

References

USEPA. 1998a. Ambient Water Quality Criteria Derivation Methodology–Human Health. Technical Support Document. Final Draft. EPA 822-B-98-005. Office of Water. Washington, DC. July.

USEPA. 1998b. Ambient Water Quality Criteria for the Protection of Human Health: Hexachlorobutadiene (HCBD). EPA 822-R-98-004.