EPA

Response To Peer Review Comments On Draft Revisions To The Methodology For Deriving Ambient Water Quality Criteria For The Protection Of Human Health

CONTENTS

CANCER/NONCANCER WORKGROUP RESPONSES

1. **Response to the Workgroup's Technical Charge Comments and Recommendations on Cancer (5.2.1)**

   Issue 1: EPA has presented a detailed discussion concerning scientific issues associated with the cancer risk assessment methodology and its intentions for incorporating the Agency's new Proposed Guidelines for Carcinogen Risk Assessment (1996). Specifically EPA requests comment on applying the new approaches to dose-response assessment and modeling to its water quality criteria program.

   The workgroup supported the EPA proposal that risks in the range of 10^{-6} are appropriate for the average person (general population) at risk and 10^{-4} for a person who is highly exposed because of specific exposure circumstances. One workgroup member also wanted EPA to present ambient water quality criteria (AWQC) at risks of 10^{-4}, 10^{-5}, and 10^{-6} instead of a single value based on 10^{-6} risk. EPA's response to this issue is discussed in the section on Exposure Assessment Workgroup Responses (in subsection 4.3, beginning near the bottom of page 21).

   The workgroup recommended that EPA use the same method for carcinogens based on a nonlinear low-dose extrapolation and noncarcinogens and combine Equations ID-1 and ID-2 for the reference dose (RfD) and point of departure/safety factor (PdP/SF) on p. 50 in the *Federal Register* notice. EPA agrees that Equations ID-1 and ID-2 are operationally similar equations. However, it is better to keep the two operations separate during analysis because PdP/SF may differ from RfD. The RfD, by definition, should be from the most sensitive noncancer endpoint.

   The workgroup wanted to see more criteria (for using the linear versus the nonlinear equations) adequately spelled out in the *Federal Register* notice and the Technical Support Document (TSD). EPA's response to this comment is stated above in the first paragraph under Issue 1.

2. **Response to the Workgroup's Technical Charge Comments and Recommendations on Inconsistencies Between Cancer and Noncancer Methodologies (5.2.2)**

   1. Application of an RfD range rather than default point-estimate

   The workgroup discussed the EPA proposal to allow the use of a point within an RfD range as the basis for deriving water quality criteria rather than the single point default estimate of the RfD. The workgroup thought that the mechanism suggested for selecting the range from which an alternate to the default RfD could be selected was not scientifically justified. They were also not certain that the flexibility offered by this option would be useful to the risk assessor.

   EPA agrees that the log-based apportionment for the range from which an RfD other than the calculated RfD can be chosen is not based on specific data. It is simply a partitioning of an order of magnitude into equal segments on either side of the calculated RfD. It is important to note that the uncertainty range about the calculated RfD establishes a domain from which a risk

assessor can select a single point to use as the alternate RfD under defined circumstances. One example of a situation where a point other than the calculated RfD might be applied would be that where there is a difference in the bioavailability of the contaminant in the water component of the AWQC as opposed to the fish component. In such an instance, the decreased bioavailability from fish tissues could be used to support selection of an RfD value greater than the calculated value if the critical study was one that administered the contaminant in drinking water.

Because the methodology says that a point within the range is selected when the uncertainty factor (UF) is 100 or greater and the range is either a quarter or half log unit to either side of the calculated RfD, it offers some flexibility for site-specific or contaminant-specific situations but remains protective of public health.

2. *Separate (yet effectively identical) methods for noncarcinogens versus carcinogens based on a nonlinear low-dose extrapolation*

The workgroup made a number of comments supporting harmonization of the cancer and noncancer methodologies, using benchmark modeling for all noncancer endpoints, and expressing RfD values in terms of risk. This cluster of workgroup comments regarding EPA methodologies for noncancer endpoints addressed issues about previously published, EPA-wide guidelines for health risk assessment or current, active projects of the agency Risk Assessment Forum to revise carcinogen risk assessment guidelines and to harmonize assessment methods for noncancer and cancer endpoints. The comments of the workgroup are noted and will be considered in the context of revisions to our assessment guidelines. The human health methodology is an application of broader EPA-wide guidelines. Revisions to fundamental Agency guidelines are beyond the scope of this document.

3. *Proposed effects on AWQC of incorporating physiologically based pharmacokinetic (PBPK) modeling for noncarcinogens vs. (linear or nonlinear low-dose extrapolated) carcinogens*

As part of a their request that EPA harmonize the cancer and noncancer approaches, the workgroup supported viewing the interspecies UFs as being made up of a pharmacokinetic and pharmacodynamic component.

We agree that both toxicokinetics and toxicodynamic differences contribute to the difference in response between animals and humans. We also accept that there are differences in opinion as to the magnitude of the UF for toxicokinetics and that for toxicodynamics.

The Peer Review Report states the Health Risk Assessment Committee (HRAC) conclusion that the toxicodynamic factor should be independent of the toxicokinetic factor and "be about the same size as the correction factor used to adjust for interspecies toxicokinetic differences."

On the default UF for extrapolation from animal dose to human equivalent dose, the workgroup recommended a "unified approach" for both carcinogens (linear and nonlinear approaches) and

noncarcinogens. The suggested approach uses two factors: a scaling factor, adjusting for toxicokinetics (UF_{A-PK}) and a UF_{A-PD}, adjusting for toxicodynamics. Thus, the UF becomes a multiplication of these two factors [i.e., $UF = (UF_{A-PK})(UF_{A-PD})$]. For carcinogens, the workgroup agreed with the use of 0.75-power of body weight to scale for toxicokinetics between species in the absence of adequate PBPK data/models. For noncarcinogens, assigning a 3 to both factors as proposed in the noncancer section of the human health methodology preserves the default interspecies UF of 10 and gives each factor equal weight. However, the workgroup recommended that UF_{A-PD} (3) also be applied to carcinogens based on linear low-dose extrapolation. This will be specifically addressed in the final carcinogen assessment guidelines. EPA has a separate ongoing effort to harmonize assessment approaches for differing endpoints, and the workgroup comments will be considered in that effort. The human health methodology is an application of broader EPA-wide guidelines. Revisions to fundamental Agency guidelines are beyond the scope of this document.

4. *Consideration of non-ingestive exposures for noncarcinogens and carcinogens based on nonlinear low-dose extrapolation versus linear low-dose extrapolation.*

The workgroup recommended using relative source contribution (RSC) for both nonlinear and linear low-dose extrapolated carcinogens. The Agency does not consider it necessary to apply another factor such as RSC for carcinogens based on linear low-dose extrapolation because of the conservatism built in a linear nonthreshold model. For carcinogens based on linear low-dose extrapolation, the method does not assume any threshold at low doses, whereas for noncarcinogens or carcinogens based on nonlinear low-dose extrapolation, a threshold is assumed below which there is no risk.

5. *In contrast to methods for noncarcinogens and carcinogens based on nonlinear low-dose extrapolation, the methods proposed for carcinogens based on linear low-dose extrapolation do not consider human interindividual variability.*

The workgroup would like EPA to consider another UF for interindividual variability for carcinogens based on linear low-dose extrapolation. EPA agrees with the National Research Council's recommendation (NRC, 1994) that "the conservatism inherent in a linear-no-threshold model obviates the need for any explicit consideration of interindividual variability in human susceptibility to environmentally induced cancer." This comment by NRC was with respect to general population exposure. The NRC recommended possible consideration of an extra factor for interindividual variability when assessing risk to a special population such as one exposed to a fenceline risk from a dispersive source of air toxics. The present methodology is more applicable to the general population. , Even though an additional factor is not considered necessary generally, specific data on sensitive subpopulations such as children, who may be particularly sensitive to a specific chemical, will be considered in risk decisions.

6. *In contrast to methods for carcinogens based on linear low-dose extrapolation, the methods proposed for noncarcinogens and carcinogens based on nonlinear low-dose extrapolation do not estimate risk.*

The workgroup stated that the method proposed for noncarcinogens and carcinogens based on nonlinear low-dose extrapolation does not estimate risk. They suggested applying a modified benchmark procedure for all carcinogens based on nonlinear low-dose extrapolation and for noncarcinogens. The benchmark dose would be associated with a specific risk of an explicitly defined adverse response. Thus, a corresponding distribution of risk could always be estimated for any specified distribution of actual or potential environmental exposures to noncarcinogens and/or carcinogens based on nonlinear low-dose extrapolation. The issue is related to Agency policy on linearity/nonlinearity and dose response, which will be addressed in the final guidelines for carcinogen risk assessment. See our discussion above in the first paragraph under Section 1, Issue 1.

3. **Response to the Workgroup's Technical Charge Comments and Recommendations on Noncancer (5.2.3)**

   Issue 1: The use of a point within the RfD range for deriving water quality criteria, rather than a single point default estimate, and the factors for determining its justification.

This charge to the workgroup related to the option for using a point within a range about the calculated RfD as an alternative for risk assessment when there was adequate justification for the alternate RfD. The workgroup's sentiments on regarding this issue and the EPA response are presented above under Section 2, item 1.

   Issue 2: Incorporating information on severity of effect, less-than-90-day studies, and Physiologically-Based Pharmacokinetic data into derivation of RfDs.

   Severity of Effect

The workgroup thought that the state of the science does not support a quantitative adjustment for severity of effect in the development of an RfD. They stated that it is not simple to determine whether adverse effects are mild or moderate and that it is often not possible to determine whether effects are reversible or irreversible from a less-than-90-day study. EPA agrees that it is difficult to quantify severity of effect in risk assessment. However, when the mode of action is known and a sequence of precursor events is well established, it may be possible to establish a quantitative relationship between a dose for a precursor event and the adverse effects and, thus, quantify the severity of the precursor event when it is used as the point of departure.

   Less-Than-90-Day Studies

The workgroup did not support using less than 90-day studies for derivation of an RfD except under unusual circumstances. In a special case where a less-than-90-day study was used, the workgroup stated that an additional UF of 10 should be added to the RfD calculation. The Agency agrees with the workgroup's suggestion that studies of less-than-90-day duration be used in the derivation of the RfD only if the reason for doing so it is carefully explained. We

disagree with the suggestion that an additional UF of 10 always be used when an RfD is based on a less-than-90-day study. If the RfD is based on an acute effect and is simultaneously protective against chronic effects, it is appropriate to use an acute study and not apply an added 10-fold UF. If the contaminant is a nutrient, a 10-fold UF applied to a NOAEL from a short-term human or animal study solely because of the duration of the study is often not appropriate.

PBPK Modeling

The workgroup supported the use of physiologically based pharmacokinetic modeling but pointed out that PBPK modeling does not account for differences in pharmacodynamics between species. The human health methodology supports the use of PBPK modeling and is in agreement with the workgroup that pharmacodynamics as well as pharmacokinetics must be considered in calculating the RfD.

> **Issue 3:** *The use of reproductive/developmental, immunotoxicity, and neurotoxicity data as the basis for deriving RfDs.*

EPA asked the peer reviewers if they believed it was appropriate to use reproductive/ developmental, immunotoxicity and/or neurotoxicity data as a basis for deriving an RfD. The workgroup responded that all relevant toxicological data should be considered in the RfD

derivation process. They agreed with EPA's concern that some immunological data are difficult to utilize in RfD development.

We agree with the workgroup's recommendation that it can be appropriate to use reproductive/developmental, immunotoxicity, and neurotoxicity data as the basis for deriving RfDs and concur with their suggestions regarding the vagaries of using certain immunotoxicity endpoints in assessment.

> **Issue 4:** *Case-by-case consideration of a nonthreshold mode of action for certain chemicals that cause noncancer effects when deriving RfDs.*

The workgroup agreed that in some cases a nonthreshold mode of action is appropriate for a noncarcinogen. However, they said that the example of nickel used in the human health methodology was not appropriate, even for a sensitized person. They thought lead would be a better example. We accept this recommendation that lead is a better example than nickel of a noncarcinogen for which a nonthreshold approach risk assessment may be appropriate.

> **Issue 5:** *Whether EPA should develop guidance for when to use each noncancer method (i.e., NOAEL, Benchmark Dose, Categorical Regression).*

The workgroup supported the development of guidance on when to select the NOAEL/LOAEL, benchmark or categorical regression methodologies for RfD development. They stated that the guidance document should address the following questions:

- < When are the data sufficient for modeling?
- < Where can the data be found?
- < When do the available data not support the development of an RfD?

Peer reviewers also expressed a strong preference for the benchmark methodology over the categorical regression methodology.

Workgroup support for developing guidance for users of the AWQHH methodology regarding the selection of an approach for derivation of a RfD for a noncarcinogen is appreciated. Experience with the benchmark dose approach is growing, and the Agency is preparing a guidance document for the methodology including a discussion on the data sets that are best suited to such an analysis. The guidance document is currently being reviewed within EPA. It is hoped that a similar document will be developed for the categorical regression methodology.

EXPOSURE ASSESSMENT WORKGROUP RESPONSES

1. Response to the Workgroup's General Comments (6.1)

EPA acknowledges the workgroup's approval of certain features of the methodology revisions. Specifically, we acknowledge the following: endorsement of the Agency specifically indicating where decisions or guidance is based in science, science policy, risk management, or, perhaps, some combination of these; the flexibility offered to States and Tribes for deriving more site-specific criteria with their water quality standards programs; and the use of examples in the TSD. Our intention is to make both the final methodology guidance and the TSD as clear and useful as possible for State and Tribal programs. To this end, we will continue to identify areas where discussion of science/policy/management issues, appropriate flexibility, and the inclusion of more examples will enable better understanding and greater utilization by all States and Tribes.

Regarding the points made in the first bullet of section 6.1 (p. 6-1) of the Workshop Summary Report, we also intend to expand on the discussion of inhalation and dermal exposures. We will cross-reference existing Agency guidelines and known State guidance documents on assessing exposures from inhalation and dermal exposures. Additionally, we plan on refining the methodology, at least to incorporate information summarizing EPA's own guidance and example assessments in the TSD that account for inhalation and dermal exposures. We also wish to respond to the following workgroup comment:

> EPA [has] finally abandoned the idea that a number can be developed from a small data set and used throughout different regions. EPA now has much more data.

EPA is required under the Clean Water Act (CWA), § 304(a), to develop national default criteria that States and Tribes may use as guidance to establish water quality standards. As such, the numerical criteria values that we develop and revise remain potentially applicable to the nation. We encourage States and Tribes to use the methodology to develop criteria based on local/regional information and believe that criteria reflecting such local conditions are desirable.

2. Response to the Workgroup's Technical Charge Comments and Recommendations (6.2)

Issue 1: The appropriateness of including inhalation and dermal exposures when deriving criteria and how they should be estimated

As indicated above, EPA intends to address inhalation and dermal exposures in greater detail. We acknowledge that the potential for these exposures exists and that an approach to accounting for them in the context of developing individual water quality criteria is appropriate. In the short term, we will cross-reference existing Agency guidance and methods for inhalation and dermal exposures. We will also consider the workgroup's recommendation for providing more specific guidance on the relevance of these exposure routes to the ambient water quality criteria in the form of future refinements of the methodology guidance.

EPA acknowledges the workgroup's comments regarding State inhalation/dermal guidelines. References to such documents (e.g., California) will be considered for inclusion in the final TSD. We also appreciate the workgroup's concept of the TSD as a "living document" and, as stated in the published draft methodology revisions (i.e., the *Federal Register* Notice), we anticipate that our future role in the program includes refinement of the revised methodology. Specifically, we anticipate that as more current data and methods become available, these would be incorporated into the methodology to reflect the latest science.

Relative Source Contribution (RSC) Recommendations

The workgroup also provided specific recommendations on the concept of RSC, which they linked to their discussion of inhalation and dermal exposures. Although the workgroup concurs that the RSC concept is an important part of the AWQC-setting process, they recommend more clarity and additional examples. EPA acknowledges that additional discussion is needed to clarify what constitutes the RSC, that is, clarifying language on what sources, routes, and pathways of exposure will be specifically considered when setting a CWA 304(a) criterion, and what data sources are appropriate. Regarding the workgroup's specific recommendations, we offer the following responses.

< EPA will add information either to the Decision Tree figure or to the text to be more explicit.

< EPA will develop a more detailed TSD that offers additional examples in order to provide further clarification on how the RSC method works; this would include addressing the Box 15 allocations that the workgroup identified. This will likely take the form of an addendum (or followup document), given the current timeline for final publication of the *Federal Register* guidance. We are committed to providing methodology guidance that will enable States and Tribes to derive site-specific criteria values, if they so choose, and will pursue this endeavor.

< EPA is limited in its ability to coordinate the RSC process with other agencies. We have discussed our RSC policy with appropriate staff from USDA and FDA, and representatives from the FDA participated in the EPA workgroup that developed the Decision Tree approach. However, the specific requirements of the CWA and EPA's particular approaches to conducting risk assessments and deriving protective water quality criteria may vary substantially from the legal requirements, science policies, and risk management decisions made by various other agencies for vastly different program goals. Therefore, the RSC process is likely not the same as that used by other agencies. EPA has coordinated with USDA and FDA regarding the use of data relevant to the exposure assessments (e.g., food consumption data, contaminant monitoring data), and will continue to do so in the future.

< It is not clear what the workgroup meant by recommending that "the RSC for non-cancer is too vague" (see p. 6-2 of the report). If this refers to the discussion of its application and what constitutes the RSC (as indicated above), EPA will work to improve the clarity of this discussion. If this statement is related to the distinction between carcinogens based on linear

low-dose extrapolation and noncarcinogens (as is the statement that follows it), we reiterate our policy on the distinction here. Specifically, different approaches for addressing nonwater exposure pathways are used in setting AWQC for the protection of human health depending on the toxicological endpoint of concern. For those that are considered carcinogens based on linear low-dose extrapolation, only drinking water consumption and fish ingestion are accounted for in the derivation of the AWQC. The RSC is not applied to nonwater sources because, for these chemicals, the AWQC are being determined with respect to acceptable incremental lifetime risk posed by a substance's presence in water, given that the estimates are considered upper-bound on potential risk, and are not being set with regard to an individual's overall cancer risk from all sources of exposure. For carcinogens with a mode of action indicating nonlinearity or for a noncancer endpoint where a threshold is assumed to exist, nonwater exposures are accounted for when deriving the AWQC. 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.

Furthermore, health-based, medium-specific criteria values based on linear low-dose extrapolation typically vary from other medium-specific values in terms of the concentration value, and often the associated risk level. Therefore, the RSC concept could not even theoretically apply unless all risk assessments for a particular carcinogen based on linear low-dose extrapolation resulted in the same concentration value and same risk level; that is, an apportionment would need to be based on a single concentration value and risk level.

The workgroup expressed curiosity about RSC and other EPA programs (the Safe Drinking Water Act [SDWA] and the Food Quality Protection Act [FQPA] were specifically mentioned). EPA explicitly stated in the *Federal Register* Notice on these draft revisions that it believes, for a given pollutant, the drinking water component of an AWQC should be consistent with the Maximum Contaminant Level Goal (MCLG) established under SDWA. We therefore propose to use similar assessment methodologies for deriving AWQC and MCLGs. The EPA Office of Water (OW) has been working with the Office of Pesticide Programs regarding their implementation of the FQPA, in order to share information on how the two offices approach addressing multiple exposure sources as part of their assessment programs (i.e., tolerance-setting, health criteria). Additionally, OW has recently been working with the Office of Air Quality Planning and Standards on issues related to aggregate exposure and cumulative risk. With each of these efforts, the EPA offices are attempting to identify areas where common policies and approaches may be appropriate.

Finally, the workgroup indicates support for use of an 80 percent ceiling with the RSC. EPA acknowledges this support. In addition to the workgroup's understanding of the possibility that "new exposures and situations will arise," we reiterate here that the ceiling also is intended to provide adequate protection for those who experience exposures (from any or several sources) higher than the available data indicate. For many of the chemical contaminants that we evaluate, the data available are not extensive.

> **Issue 2:** *The use of the USDA survey data to choose estimates of fish consumption among different population groups, in addition to decisions made on species*

designations, cooked weight values, and potential cooking-related changes to the toxicants.

<u>Use of the USDA Data</u>

EPA acknowledges the workgroup's support for the four-preference hierarchy. Regarding the workgroup's suggestion to provide guidance on how to conduct a consumption survey (in addition to guidance on analyzing the results), we have already done this. Specifically, the draft methodology revisions, in the discussion of the first preference for using local data, reference EPA's *Guidance for Conducting Fish and Wildlife Consumption Surveys* (EPA Report No. EPA/823/B-98/007).

The workgroup questioned the use of short-term data for long-term fish consumption estimates. Specifically, the workgroup stated that short-term data do not "capture 'chronic' usual intakes" and are "not appropriate to use when estimating long term exposures." The workgroup instead recommended use of the Tuna Research Institute (TRI) data, from the EPA/ORD *Exposure Factors Handbook* and estimates made in the *Mercury Study Report to Congress* (MSRC) using food frequency data from the National Health and Nutrition Examination Survey (NHANES III). The TRI data the workgroup refers to is actually the National Purchase Diary (NPD) study conducted more than 25 years ago. The NPD is the basis of the 6.5 g/day default value that EPA has historically used for fresh/estuarine fish consumption. At the 1992 national workshop that EPA conducted, one of the initial components identified for revision was the fish intake default rate. At that time, many participants considered the 6.5 g/day value to be inadequate and advocated the use of much more recent data. Dietary information suggests that consumption of fish has increased since that time because of nutritional, cultural, and other preferential choices, and EPA has endeavored to identify more recent survey data. We have received consistently strong input from many of our stakeholders (including EPA Regions, States, and Tribes) to this effect, urging an update. The workgroup's recommendation of the NPD data somewhat contradicts their statement (see p. 6-3) that "estimates are poor when the data are derived from older national surveys conducted for other purposes, but then adjusted to derive . . . AWQC."

The MSRC states that it is "rarely possible to measure a large number of days of dietary intake for individual subjects; consequently, a sample of one or several days is used to represent the true intake (Willett, as cited in USEPA 1997)." The report emphasizes that these samples are typically 24-hour recalls, 3-day recalls or records, or 7-day recalls or records. The MSRC indicates that data from such studies provide reasonable (unbiased) estimates of mean intake, but that standard deviations can be greatly overestimated. We reiterate here that the CSFII mean values are not biased; specifically, the intra-individual variation does not bias estimates of the mean intake of a population (Hegsted 1972). The estimates of the upper percentiles of per capita fish consumption based on 3 days of data may be biased upward, thereby resulting in a conservative estimate of risk. However, the extent to which this is overestimated is not known. We note that we did not exclusively analyze the CSFII data; rather the data were compared with

those of other studies (especially for recreational fisher and subsistence fisher estimates) that support our decision. The MSRC inevitably relies on the CSFII data from USDA, along with the NHANES III estimates of fish consumption patterns (from the early 1990s) for making estimates on fish consumption in the general population. The NPD data are also presented, for comparison.

EPA believes that the CSFII data are adequately representative of fish intake rates among the general U.S. population for purposes of national criteria. Although the MSRC indicates the potential for underestimating the *extent* of fish consumption due to the 3-consecutive-day limitation of the assessment, it states that the dietary recall/record assessment provides "more precise estimates of the quantities of fish consumed that [sic] would be obtained with a food frequency record." As part of the CSFII analysis, sampling weights were adjusted to account for nonresponse and were subsequently reweighted using regression techniques that calibrated the sample to match characteristics correlated with eating behavior. States and Tribes are encouraged to use local data on dietary preferences to establish criteria when national estimates are not suitable.

The *Exposure Factors Handbook* indicates the advantages of the NPD in terms of its high response rate, national representativeness, and consumption record over a 30-day period. However, according to the *Handbook*, the upper percentiles from the NPD data are (as is the CSFII) likely to overestimate the corresponding upper percentiles of long-term intake (the same is indicated for the standard deviation). According to the MSRC, there were other limitations in the NPD. For example, the survey did not include data on the quantity of fish represented by a serving (or information to calculate actual consumption of fish from numerous entries, e.g., breaded fish, fish mixed with other ingredients), and there may have been underreporting over time because of the survey diary completion requirements. Also, several studies indicate that the quantities and types of fish consumed have changed over the past 25 years. Further, comparisons between these data and newer studies are not possible because of the unavailability of the survey sample weights and participants' body weights.

Advantages of the CSFII, according to the *Handbook*, include its large sample size, representativeness, and relative currency. The *Handbook* describes it as the "key study" for estimating mean fish intake. The *Handbook* does recommend the NPD data for use in estimating long-term distributions; however, it actually recommends adjustments to the data to account for age of the data, and it presents values from a study that did exactly that. The CSFII study, however, suggests even higher increases in fish consumption than the adjusted values made on the NPD data. EPA also believes that the 3-day CSFII data are superior to the NHANES 1-day recall for characterizing fish consumption. Furthermore, the NHANES food frequency information is not useful because it does not break out the data by habitat and species (it is only divided into categories of *finfish* and *shellfish*), which are needed to estimate fresh/estuarine species intake. Given that the data are much more recent, the fact that the CSFII describes a nationally representative sample of individuals, and the strong support to revise the NPD-based default, EPA believes that the CSFII is the best source of current data available. The current draft TSD identifies the NPD as the basis of the 6.5 g/day assumption. We will consider including additional information on the NPD in the final TSD, as the workgroup

recommends.

<u>Consumption Among Minority Populations</u>

The workgroup reports that EPA's analysis of the CSFII (1994-95 data), as it appears in the MSRC, indicates that Asian populations do not consume greater amounts of fish than other minorities or whites. The workgroup specifically states that "although Asians consumed fish more frequently, the amount eaten per serving was less than in other groups, thus the intake in g/kg BW/day was less than that for other ethnic groups." Although this is true in terms of the data described in the MSRC as "per user" (i.e., similar data that are described in the methodology as "acute" consumption) and useful for an indication of meal size, the "per capita" data indicate greater consumption for Asian and Pacific Islander groups at both median and upper percentile values (see MSRC, Volume IV, p. 4-82, Table 4-67). We believe that the per capita rates are more appropriate to use for protection of human health from chronic exposures (i.e., for chemical toxicants that are of chronic health concern). Similarly, the MSRC analysis of "month-long estimates" for both fish/shellfish consumption (presented in grams/day) and mercury exposures (presented in $\digamma$g/kg/day) based on NHANES data, indicate higher intakes of both for the "other" ethnic/racial category than for either the "white/nonhispanic" or "black/nonhispanic" categories (see MSRC, Volume IV, p. 4-83, Tables 4-68a and b).

A point made by EPA in the draft methodology revisions was that local and regional studies exist that indicate that Native American, Pacific Asian American, and subsistence population groups may consume greater amounts than the general U.S. population. EPA recommended—and continues to recommend—the use of such studies where appropriate, as indicated by EPA's first two preferences in the hierarchy. This idea was strongly supported by the experts from the 1992 national workshop.

<u>Species Designation</u>

The workgroup stated that EPA's explanation of the species habitat designation for shrimp is not correct. However, the workgroup simply states that shrimp should be referred to as "anadromous." The term anadromous generally refers to a species that spawns in fresh water or near-fresh water and then migrates into the ocean to grow to maturity, or to an ocean species that similarly spawns in fresh or near-fresh waters. The life cycles of anadromous species vary in terms of whether they remain in fresh or near-fresh waters until they die or whether they return to ocean waters after spawning. As such, the description provided by EPA in the draft methodology revisions *is* correct and does not conflict with the term anadromous. EPA can add the term to the discussion when finalizing the documents. However, regardless of their anadromous status, shrimp have been included in the default value (i.e., designated as a fresh/estuarine species) because of their life cycle, as described in the draft TSD. The amount of time that shrimp spend in near-shore and estuarine waters is substantial enough to include them in the default assumption, thereby accounting for their potential to contribute to health risks if contaminated and, more importantly, ensuring the AWQC are protective regarding their consumption.

The workgroup also stated their disbelief that the "99th percentile of the salmon consumed is marine." EPA clarifies here the context of its statement in the draft methodology revisions. The USDA food codes containing salmon do not indicate the source of the salmon (e.g., landlocked freshwater, farm-raised, or wild). We based our allocation of salmon between freshwater and marine habitats on commercial landings data provided by the National Marine Fisheries Service for the period 1989 to 1991. All landings of Pacific salmon, including chum, coho, king, pink, or sockeye were assigned to the marine habitat. All landlocked Great Lakes salmon and farmed salmon received the classification of freshwater. The resulting apportionment for salmon was 1.18 percent to the freshwater habitat and 98.82 percent to the marine habitat.

Regarding the other species identified for designation by the workgroup (p. 6-4), EPA acknowledges that a limited number of freshwater fish are listed. The species listed directly reflect the consumption of the CSFII survey respondents. Therefore, the absence of striped bass or crayfish is due to the fact that neither were reported consumed. However, we intend to incorporate the CSFII data from the years 1994 through 1996, which will result in inclusion of additional species. We believe we have correctly apportioned all clam and oyster species to the appropriate habitat categories (i.e., estuarine/marine and estuarine-only, respectively). The workgroup believed that clams should be in freshwater and marine categories, and that oysters should be added to the marine category. EPA not only believes that the estuarine/marine allocation for clams is most accurate, but we also note that the non-marine designated species are included in the default intake rate regardless of whether being called estuarine or freshwater. For oysters, we are not aware of open-ocean harvesting and the designation of all oysters to the estuarine habitat is a more protective exposure assumption. Oysters may be present in waters outside of estuaries which are considered marine in terms of salinity, but these are near-shore waters to which water quality standards apply.

Use of Cooked Versus Uncooked Data

The workgroup advocated using data on uncooked fish weights "as recommended in the *Exposure Factors Handbook*." Separately, the workgroup recommended the uncooked weights "because of the bioaccumulation factor in the AWQC equations presented in the TSD and the *Federal Register*. Furthermore, chemical residue data are typically available for uncooked fish." EPA understands that chemical residue data and field-measured BAFs are usually described for uncooked fish and, thus, the uncooked fish weight is consistent with the fish tissue bioaccumulation value.

EPA has considered the pros and cons of using uncooked versus *as consumed* weights on several levels. First, the intake parameters of the criteria derivation equation are intended to capture ingestion—that is, what people actually consume and are exposed to. By and large, people consume cooked fish, and where raw shellfish or sushi were consumed by the CSFII respondents, those intakes were included in the *as consumed* weights. This assumption is also consistent with the dietary estimates based on prepared foods (not raw commodities) that are made by both the EPA pesticide program and the FDA Total Diet Study program. We also considered the "consistency" issue in the context of the fact that the CSFII survey respondents estimated the weight of fish they had consumed. Similarly, the basis of EPA's Great Lakes

Water Quality Guidance was a consumption survey of *as consumed* fish intakes.

Second, EPA considered the differences as discussed in the *Exposure Factors Handbook*—that is, the possibility of overestimating consumption but underestimating dose if the cooking process results in an increased concentration in the cooked fish (there is typically a weight loss in cooking). However, the *Handbook* fails to consider the opposite, where chemical concentration loss exceeds the loss of fish weight when cooking. The latter has been shown with chemicals that accumulate in fat tissue, as we discussed in the draft methodology revisions. As we previously stated, there are comparatively few chemicals for which measurements are available and the process is complicated further by the variability in parts of a fish where the chemical may accumulate, the method of preparation, and how the cooking process may transform the chemical. What is certain is that the mass of the contaminant will either remain constant or be reduced. The resulting concentration is harder to predict. The *Handbook* stated that it is "more conservative and appropriate to use uncooked fish intake rates." However, the *Handbook* also stated that "if concentration data can be adjusted to account for changes after cooking, then the 'as consumed' intake rates are appropriate." The *Handbook* presents both *as consumed* and uncooked values "so that the assessor can choose the intake data that best matches the concentration data that is being used." [We recommended the use of *as consumed* weights in the draft methodology revisions and an adjustment of the bioaccumulation factor for cooking loss, if information was available. Otherwise, we recommended using the *as consumed* weight along with the full bioaccumulation factor (unadjusted for cooking loss), which would produce a slightly more stringent AWQC.]

Third, EPA has received input from its stakeholders regarding potential confusion over the fact that uncooked weights are used in the Agency's fish advisory program and that having two sets of values may prove confusing to States and Tribes, as well as the general public. Furthermore, the measures of a contaminant in fish tissue samples that would be applicable to either compliance monitoring or the permitting program are related to the uncooked fish weights.

Therefore, EPA has reconsidered its position based on these facts in contrast to the fact that *as consumed* values more accurately represent actual intake. The approach of using an uncooked weight in the calculation will result in a somewhat more stringent AWQC (studies indicate that, typically, the weight loss in cooking is about 20 percent). EPA will derive its national default criteria on the uncooked weight fish intakes based on the input received, especially that from the States over the potential for confusion with the fish advisory program. In addition, EPA will provide guidance on site-specific modifications in its TSD volume on exposure assessment. Specifically, EPA will describe an alternate approach, by calculating the AWQC with the *as consumed* weight —again, more directly associated with exposure and risk—and then adjusting the value by the approximate 20 percent loss to an uncooked equivalent. Thus, the AWQC conversion to an uncooked equivalent can be consistently used with State/Tribal standards programs and still represent the same relative risk as the *as consumed* value. It is important to understand that the two approaches will not result in the same AWQC value. Whereas the second is more scientifically rigorous and, again, represents a more direct translation of the *as consumed* risk to the uncooked equivalent, it may be too intensive a process to expect of State and Tribal organizations whose resources are already constrained.

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Issue 3: *The use of separate intake and body weight assumptions (e.g., 17.80 g/day of fish and 70 kg body weight) versus assumptions that combine intake and body weight (e.g., 254.3 mg fish/kg body weight).*

The workgroup recommended combining the intake and body weight parameters, "especially if children are being evaluated," and modifying the equation to reflect this. The workgroup provided no additional rationale or advice. Presumably, they believe that combining the two will provide a more accurate estimate. When we presented the issue for review by the Agency's Science Advisory Board (SAB), the board provided the following advice:

> In theory it would be better to develop standards on a per kilogram body weight basis. However, in practice the results are not different enough to make much difference in the magnitude of AWQC. In particular, data should not be rejected because individual body weights are not available, and funds should not be allocated for collecting such data since no conceivable benefit would accrue.

EPA has also received input from its State stakeholders regarding potential confusion over combining the two parameters. Most believe that the difference in accuracy is negligible but that the difficulty in associating the units of mg/kg-BW/day with a meal size, especially for public communication and understanding, is great and, therefore, not particularly useful. Several stakeholders believed that if the data were combined as part of a study, or if a strong, demonstrated correlation between intake and body weight exists, the combined parameter should be used. We are evaluating recent information on both drinking water intake and fish intake from the 1994-1996 CSFII data and are assessing the differences between the two units of measure—including an emphasis of the differences with finer age categories for children when mg/kg-BW/day are used. [Note: SAB's comment on the unavailability of individual body weights is not an issue with the CSFII; that is, this information is available.]

EPA intends to provide tables in the final exposure assessment TSD of all fish/population categories for both grams/day and mg/kg-BW/day. EPA also intends to derive its national default criteria using grams/day (for fish) and L/day (for drinking water), along with a body weight assumption, as recommended by the States. However, EPA will refine the exposure assessment TSD to provide examples on how to derive criteria using either, including identifying situations where the latter estimate would provide substantively more accurate estimates.

3. Response to Other Issues Addressed by the Workgroup (6.3)

> *1. Monte Carlo and other statistical techniques should be used only if data support their use.*

EPA generally agrees with the workgroup's statements on the potential for use of statistical methods in assessing exposure when deriving AWQC. We intend to expand the discussion in the TSD to provide additional guidance on the complexity and limitations of using Monte Carlo and other techniques, and on the need for clear, scientifically defensible, and reproducible

analyses. Existing EPA documents will be relied upon and cited for the user's reference. In the context of exposure distributions, we will try to clarify how population segments can be protected at desired levels (see discussion on p. 6-6 of the peer review report, for complete comment).

We clarify here our position on two points from the workgroup's comments on this issue. First, the workgroup referred to using Monte Carlo to:

> give a clearer representation of the relationship of the conservative deterministic
> AWQC to the range of possible criteria that would be protective of various segments
> of the population.

Our inclusion of the discussion in the TSD addresses our potential use of probabilistic techniques to estimate exposures when deriving EPA national default criteria. However, in terms of the risk assessments, we derive criteria for the population most relevant to the toxicological basis of the RfD or cancer assessment. By basing default criteria on this population group, we are confident of protecting the overall population, especially given the conservative manner in which the RfD/cancer assessment is derived. However, we will continue to rely on values approved by the Agency (as published on IRIS) for the AWQC risk assessments and will not be publishing a "range of possible criteria that would be protective of various segments of the population."

Second, the CWA requirements and the goals of the water quality criteria program do not make the specific development of reasonable maximum exposure (RME) or maximally exposed individual (MEI) descriptors useful, as the workgroup mentioned in their report (see discussion on p. 6-8 of the peer review report, for complete comment).

> 2.   *The policy regarding incremental risk needs to be expanded (FR - pg. 163).*

It is not clear what the workgroup meant by their comments on considering background risk. Specifically, the workgroup stated (referring to the *Federal Register* Notice, p. 163, not the TSD):

> In the context of the TSD, background risk is not considered (i.e., only incremental
> risk is considered). However, background risk is considered in other documents
> when discussing drinking water. An explanation addressing why background risk
> is not considered should be provided.

The page cited from the *Federal Register* discussion refers to consideration of nonwater sources of exposure (e.g., diet, air) when setting AWQC—that is, background *exposures*—which the workgroup may be describing as background *risk*. The distinction we made was between chemical substances where the toxic endpoint was carcinogenicity based on linear low-dose extrapolation versus a nonlinear-extrapolated endpoint. The distinction is as follows: (1) For chemical substances where the toxicity basis is that of carcinogenicity based on nonlinear low-dose extrapolation or a noncancer endpoint and a threshold is assumed to exist, the resulting numerical value is thought to be a level below which the adverse effect (i.e., the

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effect the dose is based on) will not occur. Therefore, EPA will account for other common sources for the population being targeted in order to ensure that an individual's *total* exposure does not exceed that threshold level. (2) For chemicals that do exhibit carcinogenicity based on linear low-dose extrapolation, the AWQC are being set on the basis of the chemical substance's presence in the water. Nonwater sources are not considered because the criteria are protecting only the *incremental* lifetime risk posed by the chemical from this specific source, and are not being set with regard to an individual's *total* risk (of the chemical's linear-extrapolated carcinogenicity) from all exposure sources.

Contrary to the workgroup's statement in the workshop report, the drinking water program at EPA *has* followed the same approach—accounting for other exposure sources (by applying a relative source contribution factor) has not been done with carcinogens in the past, whereas accounting for nonwater exposures for noncarcinogens (most often a default value) has routinely been done. It is not clear to what "other documents" the workgroup is referring.

Regarding the workgroup's comments on using other sources of toxicological data, EPA has primarily relied in the past and continues to rely on the consensus values in the IRIS database for its risk assessment information. We believe it is acceptable for States and Tribes to use toxicological data and risk assessments outside of the IRIS database as long as the information and/or assessment has been externally peer reviewed and is either published or otherwise available to the public.   As stated in the Agency's *Peer Review Handbook*, EPA policy is to peer review scientifically and technically based products that are used to support EPA decisions (U.S. EPA 1998). Therefore, we recommend that States and Tribes follow this same approach when using toxicological data outside of IRIS to ensure that the resulting risk assessments are scientifically defensible.

3. *Federal Register Guidance Document Equations [Note: List of toxicants and populations protected also discussed.]*

EPA acknowledges the workgroup's suggestion to provide the AWQC equations in their most complex forms (i.e., "the level of detail provided in Equation 7.1.1"). As stated in the *Federal Register*, the "generalized" equations were presented to simplify understanding for the reader, with a footnote explaining the trophic level breakouts and where they appear in the documents. EPA will revise the methodology to explain the more complex forms at the first point where the criteria equations discussion appears.

The workgroup's comments on presentation of intakes based on mg/kg and modifying the equations to address different population groups (e.g., pregnant women and children) are addressed in the response to combining intake assumptions in Section 2, Issue 3, and the discussion on "various segments of the population" in Section 3.1, respectively. Apparently, one panelist described doing "an analysis in two different ways (e.g., benzene) and then choose the most appropriate one." This panelist presumably refers to conducting various exposure scenarios for different target populations and basing each criterion on the population at greatest risk. We agree with this, in principle, and are open to developing multiple estimates, where appropriate. However, as stated in Section 3.1, above, we derive criteria for the population

most relevant to the most sensitive toxicological endpoint and are, therefore, generally confident that the criteria are protective of the overall population. The workgroup also commented on specifying the population to protect and referred to EPA's assessment for lead in which EPA "wanted 95 percent of the population to have lead levels below a specific level." For a response to this issue, refer to 4.3, below.

The workgroup stated, "it would be helpful to have the list of toxins that occur in accumulated fish tissues and information was solicited for such an open-ended list." We have not currently compiled such a specific list. We listed 29 chemicals that we ranked highest priority for AWQC revisions from a larger list (that, by and large, also comprised chemicals with existing criteria) in terms of toxicity, occurrence data in fish tissue and sediments, and BAF values from the Great Lakes Initiative. Additionally, we stated that the Agency welcomed suggestions from the public at any time. If the workgroup was simply expressing their desire to obtain a compiled list as a reference, we will consider developing a list, available to the public, after the methodology is final and the overall state of the science predicting bioaccumulation merits such a list.

4. Response to Issues Considered by All Peer Reviewers (6.4)

1. *EPA needs to provide procedures for the States and Tribes to create water quality standards that do not require Federal resources or are not impeded by Federal constraints.*

States and Tribes are not impeded by any constraints in Federal resources. EPA encourages States and Tribes to develop their own AWQC to reflect local and regional conditions. This is reiterated in the draft methodology revisions (Appendix II (C)) and other policy and guidance documents related to the development of water quality standards. (See the Water Quality Standards Handbook, Advance Notice of Proposed Rulemaking at 63 *FR* 36741.)

States and Tribes are also encouraged to use their own data in the development or refinement of their criteria, whether through the EPA methodology or through other scientifically defensible methods as specified in 40 CFR 131.11(b). If a State or Tribe does not have an alternative methodology it wishes to use, components within the draft methodology may be refined based on site-specific information, such as lifetime cancer risk or fish consumption values. Where the State or Tribe chooses not to refine AWQC based on local or regional conditions, EPA publishes 304(a) criteria as recommendations for States and Tribes to use when adopting water quality criteria and for use when it becomes necessary for us to promulgate replacement Federal standards under CWA §303(c).

The revised human health methodology establishes a scientifically defensible approach to deriving §304(a) criteria for the protection of human health. This methodology may also be used by States and Tribes in the development of their own criteria based on their own data. A State or Tribe is not required to use this methodology or to adopt EPA's recommended criteria if they are able to develop alternative criteria based on scientifically defensible methods. EPA is not required to develop additional methodologies and believes that this methodology provides sufficient detail for States and Tribes to use in the development of criteria for local or regional

conditions that may occur for waters under their jurisdiction.

2. *Method to aggregate exposure from various sources (FR - pg. 180) -- The RSC approach vs. route-specific margin of exposure approaches.*

EPA acknowledges the workgroup's general support of the RSC approach and addressing aggregate exposures. EPA also acknowledges the workgroup's comments on the fact that cumulative risks are not assessed in the derivation of AWQC. The workgroup specifically expressed concern that

> The TSD does not address risks from multiple chemicals (or other threats for that matter). This situation arises when the population being protected has risks from exposure to chemicals not addressed in the AWQC criteria and standards, pathogens, air emissions, etc. EPA could address the way in which these other risks are taken into account, or explain that it cannot factor those risks in at present.

Assuming that all multiple exposures from multiple chemicals are additive is scientifically sound if they exhibit the same toxic endpoints and modes of action. We are very much aware of the complex issues and implications of cumulative risk and are developing an overall approach at the Agencywide level. Numerous publications relevant to cumulative risk can assist States and Tribes in understanding the complex issues associated with cumulative risk. These include the following:

Durkin PR, Hertzberg RC, Stiteler W, Mumtaz M. 1995. The identification and testing of interaction patterns. Toxicol Lett 79:251-264.

Hertzberg RC, Rice G, Teuschler LK. 1999. Methods for health risk assessment of combustion mixtures. In: Roberts S, Teaf C, Bean J, eds. Hazardous waste incineration: evaluating the human health and environmental risks. Boca Raton: CRC Press LLC, pp. 105-148.

Rice G, Swartout J, Brady-Roberts E, Reisman D, Mahaffey K, Lyon B. 1999. Characterization of risks posed by combustor emissions. Drug Chem Toxicol 22(1)221-240.

U.S. Environmental Protection Agency. 1999. Guidance for conducting health risk assessment of chemical mixtures. Final draft. Risk Assessment Forum Technical Workgroup. September. NCEA-C-0148. www.epa.gov/ncea/raf/rafpub.html.

U.S. Environmental Protection Agency. 1998. Methodology for assessing health risks associated with multiple pathways of exposure to combustor emissions. EPA/600/R-98/137. (Update to EPA/600/6-90/003, Methodology for assessing health risks associated with indirect exposure to combustor emissions). http://www.epa.gov/ncea/combust.html.

U.S. Environmental Protection Agency. 1996. PCBs: cancer dose-response assessment and application to environmental mixtures. National Center for Environmental Assessment, Washington, DC. EPA/600/P-96/001F.

U.S. Environmental Protection Agency. 1993. Review draft addendum to the methodology for assessing health risks associated with indirect exposure to combustor emissions. Office of Health and Environmental Assessment. Office of Research and Development, Washington, DC. November 10. EPA/600/AP-93/003.

U.S. Environmental Protection Agency. 1993. Provisional guidance for quantitative risk assessment of polycyclic aromatic hydrocarbons. Office of Research and Development, Washington, DC. July. EPA/600/R-93/089.

U.S. Environmental Protection Agency. 1990. Technical support document on health risk assessment of chemical mixtures. Office of Research and Development, Washington, DC. August. EPA/600/8-90/064.

U.S. Environmental Protection Agency. 1989a. Risk assessment guidance for Superfund, vol. 1. Human health evaluation manual (part A). EPA/540/1-89/002.

U.S. Environmental Protection Agency. 1989b. Interim procedures for estimating risks associated with exposures to mixtures of chlorinated dibenzo-p-dioxins and -dibenzofurans (CDDs and CDFs) and 1989 update. Risk Assessment Forum. March. EPA/625/3-89/016.

U.S. Environmental Protection Agency. 1986. Guidelines for the health risk assessment of chemical mixtures. Risk Assessment Forum, Office of Research and Development, Washington, DC. September. EPA/630/R-98/002.

The Agency's program offices (including OW and OPP) are also engaged in ongoing discussions on how to sort through the great complexities, methodological challenges, data adequacy needs and other information gaps, as well as the science policy and risk management decisions that will need to be made, as they pursue developing a sound strategy and, eventually, specific guidance for addressing cumulative risks. Additionally, OPP has factored cumulative risk into a recent assessment of several pesticides determined to have the same mode of action (i.e., triazine pesticides). Unfortunately, the workgroup stated that they had no specific suggestions on how cumulative risk should be factored into the derivation of AWQC. EPA can add a discussion about the concept of cumulative risk and the inadequate state of the science when finalizing the methodology documents. As a matter of internal policy, EPA is committed to refining the methodology as advances in relevant aspects of the science improve, as has been previously indicated.

The workgroup commented that EPA's RSC approach does not account for "effects that are specific to the route of exposure." The draft *Federal Register* language (p. 180) discussed inclusion of inhalation and ingestion exposures, and accounting for them either as part of the RSC or by using the RfD along with the RfC in determining an acceptable hazard index. EPA also discussed differences in bioavailability and absorption rates, including recommendations for situations where data exist and where they do not. We will expand this discussion and our position on route-specific differences in exposure, in a future addendum to the TSD. We acknowledge the workgroup's comment on the simplicity of the RSC approach versus the more

complicated but accurate approach of using both reference values (RfD and RfC). We also intend to expand the discussion on these alternatives. OW and OPP, as previously stated, are discussing issues and methods of aggregating multiple pathway exposures.

The workgroup also stated the following:

> The currently proposed Margin of Exposure (MOE) approach may be of great applicability to Ambient Water Quality Criteria Standards.

EPA believes that the MOE approach has merit as an alternative way of expressing risk and the Agency has used it for quite a while. OPP has used the MOE approach for residential exposure analyses and is considering using it for their aggregate evaluations. However, OPP continues to utilize Hazard Index and Aggregate Risk Index approaches also. Furthermore, EPA is considering using the MOE approach for assessing chemical carcinogens based on nonlinear low-dose extrapolation.

> 3. *What population (subgroup or percentile) is EPA trying to protect? What level of protection is EPA shooting for??*

The workgroup suggested that the methodology have clear policy and implementation goals on the population protected (issue also discussed separately on p. 6-10 of the Peer Review Report, where the workgroup referred to EPA's assessment for lead and the goal to have "95 percent of the population below a specific level").

EPA described in its *Federal Register* Notice issues regarding identifying the population subgroup that the AWQC are designed to protect (see Appendix III.C.1.(a) of the draft *Federal Register* Notice, p. 154). Nevertheless, we can provide greater clarity is characterizing the intake parameters used to derive the criteria in the context of the population subgroup(s), specifically describing the population segment as the *target population* or the *criteria basis population*, estimating the exposures, and discussing why we believe the criteria are protective of that segment of the population.

However, associating the derived criteria with a specific percentile is far more difficult, and such a quantitative descriptor typically requires detailed distributional exposure and dose information. EPA's *Guidelines For Exposure Assessment* (57 FR 22901, May 29, 1992) describes the extreme difficulty in making accurate estimates of exposures and indicates that uncertainties at the more extreme ends of the distribution increase greatly. On quantifying population exposures/risks, the *Guidelines* specifically state:

> In practice, it is difficult even to establish an accurate mean health effect risk for a population. This is due to many complications, including uncertainties in using animal data for human dose-response relationships, nonlinearities in the dose-response curve, projecting incidence data from one group to another dissimilar group, etc. Although it has been common practice to estimate the number of cases of disease, especially cancer, for populations exposed to chemicals, it should be

understood that these estimates are not meant to be accurate estimates of real (or actuarial) cases of disease. The estimate's value lies in framing hypothetical risk in an understandable way rather than in any literal interpretation of the term "cases."

EPA also recommended that States and Tribes consider developing more stringent criteria to protect highly exposed populations if they determined that criteria based on the general population would not be adequately protective. We will expand the discussion regarding our recommendations for States and Tribes and their flexibility in deriving their own criteria and/or adopting water quality standards.

Regarding the four conclusions described on p. 6-13, we offer the following responses.

< EPA agrees with the workgroup majority that the values for cancer effects (using the 90th percentile of fish consumption and a cancer risk level of 10^{-6}) are protective of public health. We believe the use of our fish intake assumption and drinking water intake assumption (2 L/day), along with other conservative assumptions of the risk assessment, provide an adequate level of protection for the vast majority of the population and are appropriate for use in deriving national default criteria. However, we are also aware that exposure patterns in general and fish consumption in particular vary substantially. We strongly emphasize our preference that States and Tribes use fish intake levels derived from local data, when available, instead of the default values when deriving AWQC to ensure that the level chosen will be protective of highly exposed subgroups in the population. [Note: The same idea also applies to the other exposure parameters, although available data indicate that the fish intake parameter is the most variable and, thus, the most subject to local/regional differences.] We recognized in the draft methodology revisions that risk management decisions involved with the derivation of AWQC are, in many cases, better made at the State and Tribal level. If, as the one workgroup member cautioned, a State or Tribe does not believe our default criteria would adequately protect populations that face a high risk, they have the flexibility to develop more stringent criteria for use in their standards programs.

< For subsistence fishers, EPA has not prescribed the combinations of fish intake levels and cancer risk levels that the workgroup indicates in this conclusion. We have recommended default intake rates for various higher fish-consuming populations for State and Tribal use. Again, States and Tribes have the flexibility to use any of these intake level/cancer risk combinations or use their own fish consumption data, as long as they can demonstrate that the most highly exposed population subgroup would not exceed a 10^{-4} cancer risk level. We also emphasized that approval of a Statewide 10^{-4} cancer risk level would be unlikely because of the need to ensure, and substantiate with data, that this level would not be exceeded. EPA notes that special circumstances and assessment of natural contaminants may lead to numbers outside the 10^{-6} to 10^{-5} risk range. Based on the support received from States and Tribes, we intend to finalize the methodology using the 99th percentile fish consumption rate from the CSFII survey. However, it must be emphasized that we also intend to derive our CWA Section 304(a) national default criteria based on the general population (while using the 90th percentile fish intake rate from the CSFII in an effort to protect most consumers of fresh/estuarine fish) and based on a cancer risk level of 10^{-6}.

(See our response for the fourth conclusion below, on the relation of cancer risk levels.)

< EPA believes that the criteria developed for noncancer effects will also be protective of most consumers of fresh/estuarine fish. We acknowledge that our water quality criteria do not account for cumulative exposures from multiple noncarcinogenic compounds (see response to 4.2, above). We appreciate the idea that cumulative exposure from other compounds with the same toxicological endpoint could make even the 50 percent ceiling on the RSC (i.e., the workgroup's reference to Table 2.3.27 in the TSD where a 50 percent apportionment of the RfD was used) not protective enough. As previously stated, we are not currently able to account quantitatively for specific cumulative chemical risks when deriving our national default AWQC. However, we continue to work Agencywide to develop policies on cumulative risk. We will consider further the workgroup's idea of using the RSC policy to address cumulative risk by possibly applying more conservative ceilings, where appropriate, as implied by the workgroup's comment.

< EPA's CWA Section 304(a) national default criteria serve as *guidance* to States and Tribes who must, in turn, adopt legally enforceable numerical criteria into water quality standards. States and Tribes have the option of developing their own criteria and the flexibility to base those criteria on population groups that they determine to be at potentially greater risk from higher exposures, if they so choose—although many States have adopted EPA's Section 304(a) default criteria directly into their standards. We believe that basing our 304(a) criteria on general U.S. population exposures is most appropriate, given their use as a default value for the nation as a whole. Furthermore, we cannot oblige the States to set their standards on a particular "sensitive population" because these criteria are guidance to the States, not enforceable regulations, and do not impose legally binding requirements. Nevertheless, in our methodology guidance, we recommended that States and Tribes give priority to identifying and adequately protecting the most highly exposed population by adopting more stringent criteria, if the State or Tribe determines that the highly exposed population would not be adequately protected by criteria based on the general population.

Also, we are not recommending a cancer risk level of 10^{-4}, as the workgroup suggests. States and Tribes have the option of deriving their criteria on a 10^{-6} risk level, as we propose to do with our default criteria, combined with fish consumption rates for highly exposed population groups. What we *have* stated in our methodology is that we consider establishment of criteria that will be protective of the general population at an upper-bound cancer risk in the range of 10^{-5} to 10^{-6} to be an appropriate risk management goal. However, consistent with the Agency's risk management policy in other programs, we now explicitly urge States and Tribes to ensure that the most highly exposed populations do not exceed a risk level of 10^{-4}. In this respect, we have for the first time in our water quality criteria program established a ceiling above which incremental cancer risk levels are not considered acceptable. We would disapprove any State or Tribal standard in which information indicated that greater risk levels may be experienced by such highly exposed groups.

It should be clarified that the incremental cancer risk levels are relative, meaning that any

given criterion associated with a particular cancer risk level is also associated with specific exposure parameter assumptions (i.e., intake rates, body weights). When these exposure values change, so does the risk. Therefore, the workgroup's recommendation that we "protect these communities at the same level as the general population" is not conceptually accurate. Given a criterion derived on the basis of a cancer risk level of 10^{-6}, individuals consuming up to 10 times the assumed fish consumption rate would be protected at a 10^{-5} risk level. Similarly, individuals consuming up to 100 times the assumed rate would still be protected at a 10^{-4} risk level. Therefore, with a criterion based on EPA's default fish intake rate (17.8 g/day) and a risk level of 10^{-6}, those consuming a pound per day would be protected at a 10^{-5} to 10^{-4} risk level (closer to 10^{-5}). If a criterion were based on a "95% percentile level of exposure and . . . at 10^{-6}" (as the workgroup suggests on p. 6-13), then it is likely that an average fish consumer would be protected at a cancer risk level of approximately 10^{-8}. The point here is that the risks for different population groups are not the same.

5. Response to Three Additional Related Issues (6.5)

1. Use of Reliable/Empirical/Adequate Data

EPA agrees with the workgroup's comments regarding the use of reliable, empirical data for inputs to the AWQC equation, including the need to address data adequacy. We will encourage the use of such data by States and Tribes and the generation of new data where resources allow and where the collection of new data would improve the assessment. We acknowledge the workgroup's approval of our minimum data requirements discussion and will emphasize that States and Tribes need to characterize their assessments as completely as possible, especially when the assessments are based on combinations of data that are older/newer, national/regional, and so on.

2. Encouraging State/Tribal Risk Assessments

As stated in comment-response 4.1, States and Tribes are not constrained by Federal limitations in risk assessment evaluation schedules, resources, or other factors; States and Tribes always have the option of undertaking their own evaluations to develop water quality criteria, as long as the criteria are consistent with CWA requirements. Indeed many States have derived chemical criteria values in the absence of EPA guidance for those criteria and will continue to be able to do so. We are well aware that the resources and expertise within States and Tribal authorities vary greatly and, although we encourage them to pursue their own criteria and standards development programs, we anticipate that many will continue to rely on our expertise and default criteria. We also acknowledge the workgroup's idea that some chemicals do not necessarily require intensive risk assessments, whereas other chemicals are of great importance and require greater accuracy. In this respect, we intend to devote our efforts to the development or revision of criteria for chemicals of high priority and national importance, as proposed in the draft *Federal Register* Notice.

3. Risks to Individuals and Populations

EPA agrees with the workgroup's statement that the AWQC approach should be one of "public health protection," and we have developed our methodology with the protection of human health in mind. The language contained in both the original 1980 methodology and the draft methodology revisions refers to risks, exposures, consumption rates, etc. for *populations*, and not specific individuals. The workgroup is correct that we do not explicitly assume that "protecting the individual also protects the population." However, the cancer risk estimates developed for AWQC are derived for targeting specific incremental cancer incidence and, as such, can be thought of as representing both individuals and populations—that is, a 10^{-6} cancer risk represents one additional cancer case (individual) in one million (population)—and is clearly a "defined risk-based goal" as the workgroup recommends.

In addition to deriving our default criteria to protect the general population, we have encouraged States and Tribes to identify and protect more highly exposed subpopulation groups based, in particular, on their water and fish consumption patterns. We *have* specifically referred to the following groups: adults in the general population; sport (recreational) fishers; subsistence fishers; women of childbearing age; and children. We also consider sensitive subgroups in calculating dose-response estimates and in hazard identifications, where data warrant. In this sense, we are concerned with risks to individuals (as represented by these population subgroups) and to the overall population. However, as the workgroup suggests, our approach preferentially minimizes risks to populations. We have also acknowledged that choosing intake rates for protection of a certain percentage of the general population is a risk management decision and have emphasized that in choosing a 90th percentile fish consumption value from the USDA national survey as a default (a survey of 11,912 *individuals*), we are intending to protect a majority of the population of fish consumers. We also believe that our default rates for the sportfisher/sport angler and subsistence fisher are protective of a majority of the individuals in those groups.

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Willett W. 1990. Nature of variation in diet. In: Willett W, ed. Nutritional epidemiology. Monographs in epidemiology and biostatistics, vol. 15. New York/Oxford: Oxford University Press, pp. 34-51. [Cited in the Mercury Study Report to Congress, 1997. EPA /452/R-97/006.]

BIOACCUMULATION WORKGROUP RESPONSES

This section contains EPA's response to all comments of the Bioaccumulation Workgroup on the bioaccumulation factor (BAF) portion of the human health AWQC methodology as contained in Section 7 of the September 1999 Peer Review Summary Report. Section 7 contained the combined comments from the workgroup on the BAF portion of the proposed AWQC methodology.

1. **Response to the Workgroup's Technical Charge Comments and Recommendations (7.1)**

    General Issue: EPA requests comment on the recommended methodology guidance for estimating BAFs using a tiered approach that depends on the availability of data and resources, and the choice of the default parameter values provided.

    General Comments

The workgroup stated that they were in general agreement that using BAFs can result in better predictions of bioaccumulation than BCFs for some nonpolar (nonionic) organic chemicals and that the choice of most of the default parameters appears generally to reflect the state of the science. However, the workgroup expressed concerns that the draft BAF methodology is much more complex and includes more assumptions than the previous BCF methodology. The workgroup also stated that many model parameters were highly uncertain and some assumptions have a tenuous scientific basis. In addition, the workgroup said that, as written, the draft methodology has only had limited testing and could not be applied to ionizable compounds (e.g., pentachlorophenol).

We agree with the workgroup that BAFs are better predictors of chemical accumulation than bioconcentration factors (BCFs) for certain types of compounds such as highly persistent, highly hydrophobic chemicals. Numerous studies have confirmed the finding that for some chemicals, BAFs exceed BCFs because of food web biomagnification (e.g., Russell et al. 1999; Fisk et al. 1998; Oliver and Niimi 1983, 1985, 1988; Niimi 1985; Swackhamer and Hites 1988). We further agree with the reviewers that for some compounds (e.g., nonionic organic chemicals that exhibit relatively low hydrophobicity), the BAF is expected to be similar to the BCF. To address this issue, we have revised the 1998 draft BAF methodology so that BAFs and BCFs for minimally hydrophobic organic chemicals are considered equally in determining the National BAF for an aquatic species, all else being equal.

We appreciate the need to balance complexity versus simplicity in developing guidance for assessing bioaccumulation for deriving AWQC. The 1998 draft bioaccumulation methodology is more complex than the 1980 methodology, which emphasized the use of measured BCFs or BCFs predicted from K_{OW} values. However, significant scientific advancements have occurred over the past 20 years that have greatly expanded our understanding of the bioaccumulation process. Therefore, the added complexity of the draft methodology is required to increase the scientific soundness and accuracy of AWQC through incorporation of these scientific advances.

For example, methods to directly address the effect of organic carbon on the bioavailability of nonionic organic chemicals are absent from the 1980 methodology but are explicitly incorporated in the revised bioaccumulation methodology. Furthermore, the use of model-derived food chain multipliers in combination with measured or estimated BCFs has been shown to provide more accurate estimates of bioaccumulation for persistent, highly hydrophobic chemicals than the use of BCFs alone (Burkhard et al. 1997; U.S. EPA 1995, 1998). These methods are also absent in the 1980 methodology. In addition, trophic-level dependence of bioaccumulation, which can be important for some types of chemicals, is not explicitly addressed in the 1980 methodology but is addressed in the new methodology. It should be noted that the added complexity of the revised 2000 methodology also provides greater opportunity to stakeholders to modify national BAFs to address site- or region-specific attributes, which again was lacking in the 1980 methodology.

We agree that for some types of chemicals, the procedures for deriving BAFs can be simplified from those presented in the 1998 draft methodology. Accordingly, we have revised the 1998 draft methodology so that the derivation of BAFs is tailored to specific categories of chemicals, some of which require less complex procedures. For example, we revised the draft methodology to limit the use of food chain multipliers (FCMs) to groups of chemicals where they are most likely to impact the BAF (e.g., highly hydrophobic organic chemicals that have reasonable likelihood of persisting in aquatic biota). We do not recommend use of FCMs for other types of chemicals (e.g., organic chemicals that have been shown to metabolize substantially in biota and those with low hydrophobicity). We have also limited the derivation of separate BAFs for each trophic level to groups of chemicals where such distinctions are most meaningful (e.g., highly hydrophobic chemicals).

Responses are provided below for the various comments pertaining to model parameters and assumptions.

< Evaluation of the draft bioaccumulation methodology focused on persistent, hydrophobic chemicals in selected locations (e.g., Lake Ontario, Green Bay, Bayou d'Inde, Louisiana) because of a general lack of appropriate data for other types of chemicals in other geographic areas. The workgroup raised concerns about the applicability of certain portions of the methodology to certain classes of chemicals. In response to this, we have developed additional guidance that restricts some aspects of the methodology to certain types of chemicals. For example, we have removed the use of K_{OW}-based BAF estimates and model-derived FCMs for chemicals that have been consistently shown to be metabolized substantially in aquatic biota (e.g., benzo[a]pyrene in vertebrates).

< Regarding the locations in which certain aspects of the methodology have been tested (FCM and biota-sediment accumulation factor (BSAF) approach), we agree that these sites are few in number, largely because the availability of appropriate field data is so limited. Although few in number, these sites do provide a range of ecosystem types from which to evaluate the BAF methodology. Specifically, they include the hydrodynamically complex and tidally influenced area of Bayou d'Inde (Lake Charles, LA) and the more stable, oligotrophic system of Lake Ontario. A limited evaluation of the BSAF methodology was

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also performed with the more shallow, eutrophic system of Green Bay, Lake Michigan. To obtain an assessment of the performance of the BAF methodology in lotic systems, we evaluated two other data sets (PCBs in the Hudson River and Fox River/Green Bay). We believe that placing additional limitations on the use of predicted BAFs, as noted above, and the further evaluations we conducted to compare predicted BAFs in other systems (e.g., Hudson River and/or Fox River/Green Bay) to field-measured BAFs, give the revised bioaccumulation methodology a better scientific foundation and supports using it to derive national BAFs.

<   Regarding ionizable chemicals, we agree that the draft methodology did not clearly differentiate between nonionizable and ionizable chemicals and have revised the draft methodology to include separate procedures specific to determining BAFs for ionizable chemicals.

Document Readability

The workgroup stated that the bioaccumulation methodology needed revision before it could be applied on a national scale. Specifically, the methodology needed better direction and improved readability, including a more precise description of what to do and when to do it. The workgroup recommended that a more prescriptive approach be developed that retains the intended flexibility and site-specific alternatives. In one instance the workgroup also commented that once revised, the methodology might be implemented on a more limited State or site-specific scale.

EPA has made substantial revisions to the 1998 draft bioaccumulation methodology as a result of workgroup comments. To improve readability and clarity of the methodology we separated the guidance for developing national BAFs from the guidance for developing site- or region-specific BAFs. The revised national BAF methodology is written in a more prescriptive manner so that it is clear how EPA plans to derive national BAFs. In the guidance for site- or region-specific BAFs, we have expanded the guidance to better enable such adjustments to be made by States, Territories, and authorized Tribes. For example, the databases used to develop national default values for lipid content in aquatic biota and organic carbon content in water were updated and expanded to make data more accessible so that States and authorized Tribes can more readily develop site- or region-specific values. After publication of the revised methodology, we will also develop detailed guidance to stakeholders for designing and conducting field studies to measure site-specific BAFs and BSAFs. This guidance will specify our recommendations for how, when, where, and how often one should sample water, biota, and sediment for producing reliable measurements of BAFs and BSAFs. We expect to complete this guidance within a year following publication of the revised AWQC methodology.

In addition to improved clarity and expanded guidance, we have revised the draft bioaccumulation methodology to address and reduce uncertainty in various aspects of the methodology, as recommended by the workgroup. For example, to reduce uncertainty in national BAFs as a result of improper application of the methodology to a certain chemical group, and to simplify procedures, we developed separate procedures for deriving BAFs for

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different chemical classes (e.g., high versus low hydrophobicity, high versus low metabolism in biota, ionic versus nonionic organics). We also revised the guidance to recommend that K_{OW}-based estimates of BAFs and FCMs not be used for nonionic organics that are known to be metabolized substantially in targeted biota. Restrictions have been put on the use of the BSAF methodology, such that it is applied only to highly hydrophobic organic chemicals.

Scale of Application

Although we recognize that even with the revisions to the BAF methodology, significant uncertainty might exist in the derivation and application of national BAFs at some sites throughout the United States because of the influence of site-specific factors, we do not agree that the methodology should be limited to State or site-specific use. We believe the revised methodology is applicable on a national basis and will result in broadly applicable national BAFs for several reasons. First, for the predictive methods that incorporate factors affecting bioavailability and bioaccumulation (i.e.,DOC/POC, lipid) we use default values for the factors based on average values derived using large nationally representative data sets. Second, we obtained bioaccumulation field data for a representative range of ecosystems (e.g., Lake Ontario, Green Bay/Fox River, Hudson River, Bayou d'Inde), chemicals (PCBs, dioxins, chlorinated benzenes, pesticides), species, and trophic levels and shown through comparisons of field-measured and predicted BAFs, that when used appropriately, the different predictive methods result in BAFs that agree very well to field-measured BAFs with few exceptions. Third, by improving the readability and direction of the bioaccumulation methodology and by limiting the use of the different BAF methods to certain groups of chemicals for which they are most appropriate, we have also reduced the potential uncertainty that might occur from inappropriately applying the methodology to certain groups of chemicals.

We believe that deriving national 304(a) water quality criteria using national BAFs is a sound scientific approach and results in criteria that can be implemented effectively throughout the United States. For more than two decades, EPA has developed and implemented its national 304(a) water quality criteria (aquatic life and human health) through State and, on occasion, Federal water quality standards programs. Implementation of this program has relied on the use of national 304(a) criteria as a cornerstone, and has evolved to allow the use of procedures to modify national criteria by States, Territories, authorized Tribes, and other stakeholders where appropriate. The revised national bioaccumulation methodology is consistent with this programmatic practice, by enabling States, Territories, and authorized Tribes to readily adopt national 304(a) water quality criteria into standards (based on national BAFs) that achieve the Clean Water Act goals of protecting public health while also allowing site- or State-specific adjustments to be made in situations where national AWQC may be considered to be overprotective or in some cases, underprotective. In contrast to the workgroup recommendation, we believe that restricting the bioaccumulation methodology only to the development of State or site-specific BAFs would greatly hinder implementation of water quality criteria throughout the United States. This would be the case because many States, Territories, and authorized Tribes lack the resources to develop State- or site-specific BAFs for all of the numerous pollutants of concern and thus, subsequent adoption of AWQC would be delayed

substantially.

> **Issue 1:** *The appropriateness of the recommended procedures for estimating the consumption-weighted default lipid value, the equation to derive the freely dissolved fraction of a chemical (including estimates of K_{DOC} and K_{POC}), and the choice of food web structures used to calculate food chain multipliers.*

Default Lipid Value

The workgroup stated that the general approach for deriving the default lipid level is appropriate but had several concerns that led them to question the representativeness of the trophic-level mean lipid values. One concern related to the low or unknown sample sizes of lipid values supporting many of the species-mean lipid content values. Although the workgroup was unaware of any other compilation that EPA could use to augment its existing database, they indicated that individual studies that report lipid content could be used to provide a more robust database.

EPA agrees that several data sets supporting the species-specific lipid values are of low or unknown sample size because of limitations in the available data. Most of these data sets pertain to the estuarine species, which are not widely represented in available databases, such EPA's environmental monitoring database called STORET (data STOrage and RETrival). STORET is a repository for water quality, biological, and physical data and is used by state environmental agencies, EPA and other federal agencies, universities, private citizens, and many others for environmental management purposes. Generally, the sources used for estimating lipid content for estuarine species report data in summary format and do not reveal the underlying sample size. In order to increase the certainty of species-mean lipid values, we have conducted additional data searches that specifically target lipid data for species where the sample size is low or unknown. Where appropriate, we have expanded the data sets to include additional data for these species.

Another workgroup concern regarding the representativeness of the recommended national default lipid fraction values related to the aggregation of lipid data to the trophic level category, including both freshwater and saltwater species, given the variability in lipid content that can occur within and across species in the same trophic level. The workgroup recommended that additional guidance be developed on how site-specific data could be combined with the national default data.

As discussed in the 1998 draft bioaccumulation methodology TSD, lipid content can vary significantly not only across aquatic species but also within a species because of a variety of factors, including age, size, sex, and diet of the fish; sampling season; and environmental conditions (pp. 185, 239). Furthermore, the representativeness of the national default values may vary for different sites. As a result, we recommended (and will continue to recommend in the revised national bioaccumulation methodology) that wherever possible, States, Territories, and authorized Tribes use site-specific or region-specific data to determine the identity and lipid

content of consumed aquatic species. To enable States, Territories, and authorized Tribes to develop their own lipid content estimates, we have revised the lipid database used in the 1998 draft methodology. The new lipid database includes more data for aquatic species having low sample sizes (see previous response to comment) and to include additional aquatic species that may be commonly consumed but were not part of the original database. Such species (e.g., walleye) were usually omitted from the database in the 1998 draft methodology because they did not reflect the types of aquatic biota that were being consumed by humans as reported by the USDA's Continuing Survey of Food Intake by Individuals–CFSII, 1989-1991. We expect the revised and expanded lipid database to be much more useful to States, Territories, and authorized Tribes when they are modifying the national default lipid content values to better reflect their situation.

States, Territories, and authorized Tribes will not always have the resources or data to develop site- or region-specific lipid values. In these situations, the national values provide States, Territories, and authorized Tribes with reasonable default values of lipid content in commonly consumed aquatic organisms based on the best available data. Regarding aggregation of lipid content data to the trophic level, it should be noted that the mean lipid fraction value determined for each CFSII consumption category in the 1998 draft methodology was weighted appropriately by the corresponding consumption rate determined from the survey. For example, variation in mean lipid content between the CSFII category of "perch" and "estuarine salmon" (both assigned to trophic level four) was accounted for in the national default lipid value calculation by weighting by their individual consumption rates. In recognition that lipid content can vary appreciably across species comprising each of the CSFII consumption categories (e.g., lake trout versus brook trout in the "trout" category), we derived "average," "low," or "high" estimates of the recommended national default values in the draft 1998 methodology, based on differing assumptions of the representativeness of different species for a given trophic level. Although these estimates were originally done as a sensitivity analysis, we have added additional guidance to States, Territories, and authorized Tribes in the TSD on how to adapt the national default lipid values to reflect State and local consumption patterns where such data are available. To enable such modifications to be made, we will make the raw data available to States, Territories, and authorized Tribes for the purposes of selecting species-specific lipid content different from the default values used by EPA in derivation of national 304(a) criteria.

The workgroup had several comments concerning the method of lipid extraction and analysis. These concerns include (1) not specifying the lipid extraction method used for data constituting the national default lipid values, (2) the need to recommend method(s) for measuring lipid composition, including what tissues to analyze, and (3) a recommendation that alternative (but unspecified) lipid extraction methods used for fish residue analysis would be more appropriate than the Bligh-Dyer method, due to its greater affinity for polar lipids.

As discussed on page 185 of the 1998 TSD, various lipid extraction methods can extract differing quantities of lipid from the same tissue of aquatic organisms. In one study (Randall et al. 1991), lipid fraction varied by nearly fourfold among four extraction methods, but varied by twofold or less among two of the more common extraction methods (chloroform-methanol and acetone-hexane). Additionally, the relative importance of lipid extraction method might vary

depending on the lipid content of the tissue, with lean tissues containing proportionally more polar lipids (and greater potential difference due to the type of extraction solvent used) compared with tissues with more adipose (nonpolar) lipids. Other attributes (e.g., high temperature, pH, lipid decomposition due to exposure to light and oxygen) also can affect lipid extractions.

Although it is desirable to have one standardized method for extracting and analyzing lipids for the purposes of normalizing residues of nonionic organic chemicals, a clear consensus has not emerged on which method is most appropriate for all tissues, species, and nonionic chemicals. Furthermore, it might be true that no single method is equally appropriate for all chemicals and tissues because different tissues have different lipid compositions (e.g., polar versus nonpolar lipids), which in turn may alter the partitioning of various nonionic organic chemicals to varying degrees. The science is not presently clear on which lipid fractions (e.g., phospholipids, free fatty acids, mono-, di- and triglycerides) are most toxicologically relevant with respect to different organic chemicals. For example, DDT has been reported to bind to more polar membrane-associated lipids, which might render them toxicologically relevant (Chefurka and Gnidec 1987, as cited by Randall et al. 1991). In a followup study, Randall et al. (1998) reported that 27% of extractable PCBs were analytically associated with the more polar, membrane-bound lipid pool (i.e., extractable with chloroform/methanol) whereas 73% were associated with the neutral lipid pool (i.e., extractable with hexane). This finding further suggests that membrane-bound lipids should not be ignored with lipid extraction techniques, at least for some pollutants.

Although there is practical appeal to using the same solvent system to extract both lipids and nonionic organic chemicals (i.e., separate chemical and lipid extraction methods would not be necessary, as is required with the Bligh and Dyer method), different analytical methods can vary in their extraction methods even for the same pollutant. For example, EPA method 1613 for chlorinated dioxins and dibenzofurans uses a 50:50 mixture of hexane:methylene chloride to extract fish tissues (U.S. EPA 1994). Another EPA method for analyzing PCBs and TCDD for fish tissue uses acetonitrile (U.S. EPA 1980). Thus, coextraction of lipids with the target analytes may still result in different lipid fractions being measured for the same tissue, depending on the analytical method used. Furthermore, as noted above, it is not clear that the more polar lipids (e.g., membrane-bound phospholipids) are toxicologically irrelevant.

For the sake of consistency in measuring BAFs and BSAFs using field studies, we continue to recommend the use of the Bligh and Dyer (1959) chloroform/methanol extraction method (or the less toxic solvent system of Hara and Radin (1978) which uses hexane/isopropanol) in combination with gravimetric analysis for lipid measurement (p. 185 of TSD). We recommend the Bligh-Dyer method because it is widely used for lipid measurements and has been well characterized in terms of the types of lipids extracted. The Bligh-Dyer method also extracts both polar and nonpolar lipids, both of which might be toxicologically important. These and other considerations led Randall et al. (1998) to recommend the Bligh-Dyer method as a standard technique for total lipid extraction pending more research to identify the complex neutral pollutant and lipid relationships and subsequent development of a final standard method. Randall et al. (1998) further recommended that if other lipid extraction methods are used, comparisons

should be made to the Bligh-Dyer method to allow conversion of the lipid results to Bligh-Dyer equivalents. EPA has added similar guidance in the revised bioaccumulation methodology.

Regarding the tissues to be extracted, we have added guidance recommending that the percent lipid be measured on the tissue used to derive the BCF or BAF study, which should be the edible tissue of the organisms (e.g., fillet, whole body, soft tissue, etc., depending on the species). Guidance was provided on the preferred tissue type on pages 175 and 185 of the draft 1998 TSD, and we have added clarity to this language.

Finally, where data were available, we have summarized which lipid extraction methods were used to develop the database that supports the recommended national default lipid values. We reviewed the lipid data and removed data derived using methods that were considered to be suspect. It should be noted, however, that we weighed the added uncertainty of basing national default lipid values on substantially fewer lipid data (because of incomplete information on extraction method) against the uncertainty that might result from including data with different or unknown lipid extraction methods. In some cases, lipid records contained little or no information on the extraction method, yet they were retained (appropriately flagged) in the database used to derive the national default lipid values.

The workgroup recommended that the tissue type (edible, fillet, whole-body) be specified on Table 2.4.8 and 2.4.10 in the TSD. We agree and have made this change.

The workgroup stated that use of the consumption-weighted default lipid value in the AWQC estimation process assumes that each trophic level is contaminated at the highest allowable concentration. The workgroup considered this assumption not realistic and recommended that some method to provide a distribution of contamination be used, or at least a differential source-based contamination scheme for separating fish from waters of concern versus fish from other sources.

As authorized by Section 304(a) of the Clean Water Act (CWA), EPA is charged with developing water quality criteria that reflect the latest scientific knowledge of the effects of pollutants on human health and welfare. EPA's 304(a) water quality criteria are often used by States, Territories, authorized Tribes, and EPA to set enforceable water quality standards that are designed to meet the designated uses of a water body (e.g., fishing, swimming, propagation of aquatic life, recreation). In developing the methodology for deriving human health criteria, we made estimates about exposure to contamination from eating fish taken from surface waters. The purpose of the estimates was to ensure that if criteria were met in a water body designated for fishing, most people could safely eat fish from that water body. In addition to the estimate that 17.8 grams of fish are consumed per day (a value reflecting the 90th percentile of the general population), we also estimated that fish and shellfish are taken from water with pollutant concentration at the criterion level. It is our view that to ensure that people can safely eat fish from waters designated for fishing, it is necessary to assume that all of the consumed fish are taken from water bodies with chemical concentrations present at the criteria level (i.e., contaminated to the maximum safe level). Fishing patterns (i.e., extent and location of fishing), and the degree to which fish and shellfish bioaccumulate contaminants from waters across the

United States, may differ from the exposure assumptions used to calculate national 304(a) criteria. The national criteria (which States, Territories, and authorized Tribes may modify) are designed to be protective for the general population.

The data do not exist to enable 304(a) criteria to reliably account for the myriad of spatial and temporal differences in fishing patterns, bioaccumulation, and subsequent differences in exposure to fish contaminants at the national level. For example, a particular water body might not be of concern to individuals of one subpopulation because they do not use it for fishing. However, this waterbody might be of concern to individuals of another subpopulation because it serves as a significant resource for their diet. Data at the national level that would enable such fine distinctions to be made are not available. It should also be noted that, once adopted into State or Tribal standards, AWQC must protect the designated use of the water body (e.g., fishable, swimmable) regardless of the extent to which that designated use is actually being exploited. For these reasons, we believe that the exposure assumptions use to derive national 304(a) criteria are necessary to achieve adequate protection of humans from exposure to waterborne pollutants. Where States, Territories, and authorized Tribes have concerns regarding the level of protection afforded by EPA's national criteria, EPA encourages States, Territories, and authorized Tribes to make appropriate adjustments to reflect local conditions affecting fish consumption and bioaccumulation. Guidance for making such modifications is provided in the revised methodology.

Freely Dissolved Fraction

The workgroup commented that the equation to estimate the freely dissolved fraction of nonionic organic chemicals generally reflects the current state of knowledge, but they were concerned that the equation did not allow for ionization despite unspecified methods being available to account for this phenomenon.

The workgroup concurred with the use of the three-phase partitioning model to estimate the freely dissolved concentrations of nonionic organic chemicals in ambient waters. They suggested that the three-phase partitioning model can be extended so that ionizable chemicals such as pentachlorophenol, silvex, "-naphthylamine, and aniline can be addressed.

In response to the workgroups comments regarding ionization of organic chemicals in water, we revised human health methodology by dividing the chemical universe into three general classes: nonionic organics, ionic organics, and inorganics including organometallics. Ionic organics include chemicals containing functional groups with exchangeable protons such as hydroxyl, carboxylic and sulfonic groups, and functional groups that readily accept protons such as amino and aromatic heterocyclic nitrogen (pyridine) groups. In the revised methodology, the users are directed to the section on ionic organics when the chemical of interest is of this class, and this section also provides methodologies for deriving AWQC for this class of chemicals.

As part of the revisions, we reviewed the literature describing ionization of organic chemicals in water. In general, most organic acids, (e.g., pentachlorophenol and silvex) exist mostly in the ionized form in ambient waters because their pKa's (4.75 and 3.07) are much smaller than the

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pH of the ambient waters. Conversely, most organic bases (e.g., aniline) exist mostly in the un-ionized form in ambient waters because their pKb's (4.63) are much smaller than the pH of the ambient waters. When the species of the chemical is predominately in the un-ionized form, the chemical can be treated as if it were a nonionic organic chemical. Significant ionization (more than 99% ionized) occurs for organic acids and bases when the pH > pKa + 2 and pH < pKb + 2, respectively.

During the revisions we also reviewed available models for predicting the partitioning and bioavailability of ionized forms of organic chemicals (e.g., for review, see Spacie, 1994; Suffet et al., 1994). Although the neutral species of ionic organic chemicals are thought to behave in a similar manner as nonionic organic compounds (e.g., partitioning to lipids and organic carbon as a function of hydrophobicity), the ionized (cationic, anionic) species exhibit a considerably more complex behavior involving multiple environmental partitioning mechanisms (e.g., ion exchange, electrostatic, and hydrophobic interactions) and a dependency on pH and other factors including ionic strength and ionic composition (Jafvert et al., 1990; Jafvert 1990; Schwarzenbach, et al., 1993). As a consequence, methods to predict the environmental partitioning of organic cations and anions are less developed and validated compared to nonionic organic chemicals (Spacie, 1994; Suffet et al., 1994). Given the current limitations in the state of the science for predicting the partitioning and bioaccumulation of the ionized species of ionic organic chemicals, EPA has decided not to extend the freely dissolved equation to include ionic organic chemicals. Rather, EPA has developed separate procedures for addressing bioaccumulation of ionic organic chemicals which depend on the extent to which the fraction of the total chemical is likely to be represented by the ionized (cationic, anionic) species in U.S. surface waters. When a significant fraction of the total chemical concentration is expected to be present as the ionized species in water, procedures for deriving the national BAF rely on empirical (measured) methods (i.e., field BAF or laboratory BCF). When an insignificant fraction of the total chemical is expected to be present as the ionized species (i.e., the chemical exists essentially in the neutral form), procedures for deriving the national BAF follow those established for nonionic organic chemicals, which address the freely dissolved form. As the science improves on predicting the partitioning and bioavailability of ionic organic chemicals, EPA plans to consider the use of partitioning and bioavailability models on a case-by-case basis.
Additional information on partitioning of ionic organic chemicals is presented in the revised methodology for ionic organics.

The workgroup commented that implicit decisions and assumptions are used with the three-phase partitioning model for estimating the freely dissolved concentration for a nonionic organic chemical in the ambient water. The workgroup recommended that the guidance document needs explicitly to identify these assumptions, and to provide discussion and information "at a level that will allow the user to gain a sense of the uncertainty of this approach." The peer reviewers recommended that this detailed discussion be placed in an appropriate appendix.

Three implicit assumptions in the methodology were highlighted by the workgroup:

< The values for the particulate and dissolved organic carbon partition coefficients are set to default values depending on the type of aquatic environment.

< The assumption that the freely dissolved chemical in the water is in equilibrium with particulate organic carbon (POC), dissolved organic carbon (DOC), phytoplankton, and zooplankton.

< Chemical bioavailability to aquatic organisms is reduced because of sorption of the chemical to DOC and POC.

EPA has provided more detailed discussions and information highlighting the uncertainties associated with the implicit assumptions used with the three-phase partitioning model in the bioaccumulation factor part of the TSD. As suggested by the workgroup, we conducted an up-to-date literature review and subsequent evaluation of the default values for K_{DOC} and K_{POC} values. In the methodology section of the guidance document, we more clearly identified the implicit assumptions and refer the reader to the appropriate appendix for additional details. Where default values were used in the methodology for individual parameters, these selections/decisions have also been more clearly identified.

Food Chain Multipliers

Clearer guidance on use of FCMs. The workgroup commented that although EPA provided three different examples of FCMs that varied depending on the mix of pelagic and benthic components, no clear guidance was provided on which one to use.

The lack of clarity in the draft methodology was caused in part by mixing of the national and site-specific methodologies in the same guidance. To address this issue, in the revised methodology we have divided the national and site-specific BAF methodologies into separate documents. The detailed technical basis for the methodologies appears where appropriate in the revised national and site-specific BAF guidance documents.

For derivation of national BAFs, we chose to use a mixed benthic/pelagic food web because we believe that this food web is the most broadly applicable and typical food web encountered in nature. The use of a mixed benthic/pelagic food web also results in FCMs that are midway between a pure pelagic and pure benthic food web structure. Discussions have been provided in the revised methodology that allow the user to gain a sense of the uncertainties associated with using the mixed benthic/pelagic food web as the default food web.

For determination of site-specific BAFs, the document provides additional guidance on which of EPA's recommended FCMs to use depending on the situation. In addition, EPA also strongly recommends that site-specific FCMs be determined whenever possible using site-specific food web parameters (e.g., diet, lipid content, and weight for each organism and sediment-water disequilibrium). The revised document provides guidance on how one might assess the diet, lipid content, and weight for organisms at their field site.

Applicability of FCMs. For several reasons, the workgroup commented that the proposed FCMs are not broadly applicable to all chemicals and all aquatic ecosystems. Specifically, the

workgroup said that further validation of FCMs was needed for additional chemicals and diverse systems before FCMs could be used on a national scale. In addition, concerns were raised that the FCMs should not be applied to chemicals that are readily metabolized or those that do not reach steady state in the food chain during the same time as the environmental half-life.

EPA has revised the guidance to limit the use of FCMs, which account for biomagnification processes in aquatic food webs, to high K_{OW} nonionic organic chemicals that have been shown to persist (or have a reasonable likelihood of persisting) in aquatic biota of concern. The workgroup suggested that FCMs should not be used on a national scale. However, the workgroup did not provide alternative recommendations on how to account for biomagnification processes on either a national scale or a site-specific basis, and EPA does not know of any other sound approaches to account for biomagnification processes. (Note that FCMs and BMFs [biomagnification factors] are the same approach because BMFs are equal to ratio of FCMs. Also, it should be noted that FCMs were derived using food web models, and thus food web models and FCMs are one and the same approach as well.)

The workgroup suggested further field verification of the use of FCMs because a wide diversity of ecosystems have not been included. EPA has performed successful verification studies in two different ecosystems: (1) Lake Ontario, an oligotrophic freshwater ecosystem, and (2) Bayou d'Inde, Lake Charles, LA, an estuarine ecosystem with variable salinities. We have also evaluated additional data from the Hudson River and the Fox River/Green Bay ecosystems to further field verify the predicted BAF methods, as was suggested by the workgroup.

EPA agrees with the workgroup that FCMs that assume no metabolism in the food web could be inappropriate for chemicals that are metabolized. However, as stated by the workgroup, "there is no reliable, broadly applicable (universal) approach to predicting the metabolic breakdown of organic chemicals by biota." In view of the lack of methodologies for predicting metabolism, EPA has made a science policy decision to assume no metabolism when deriving FCMs. For chemicals and species wherein metabolism has been shown to be important, EPA has revised the guidance to recommend not using model-derived FCMs. EPA has added text and guidance caveating the limitations of the FCMs because of their inability to account for metabolism processes. In the methodology, BAFs derived using the product of a measured BCF and FCM do include metabolic processes of the organisms used in the BCF measurement. The revised BAF methodology allows modification of the national BAFs to account for site-specific applications, which includes procedures to account for metabolism in the derivation of site-specific FCMs when appropriate metabolic rate data exist.

The workgroup suggested that "chemicals that do not reach steady-state in the food chain during the same time frame as the environmental half-life should not be included here." We do not agree with this because the suggestion does not recognize that time to steady-state and environmental half-life are not necessarily related. In addition, loadings of the chemical to the ecosystem are an important and controlling factor in establishing the concentrations of the chemical in the ecosystem (e.g., ambient water). Consider the following example: Assume that one unit of a chemical is added to a lake per day, the lake is well mixed, all chemical is retained in the lake, and the chemical is lost using a first-order rate loss. Given enough time, the total

amount of chemical in the lake will plateau at 43.8 units assuming a 30-day environmental half-life for the chemical. Because the total amount of chemical in the lake plateaus, the time to steady-state in the food web has no relevance to whether the residue is formed or not formed in the organisms composing the food web. As one decreases the environmental half-life of the chemical, the total amount of chemical in the lake becomes less; for example, for environmental half-lives of 10, 5, and 1 days, the total amounts of chemical in the lake are 14.9, 7.7, and 2.0 units. When the environmental half-life becomes very small, less than 1 day in this example, the total amount of chemical in the lake becomes very small, e.g., <<1 unit. Even when the environmental concentrations become very low, bioaccumulation processes still occur. In effluent-dominated systems, bioaccumulation of chemicals with relatively short environmental half-lives might be important because of the continuous loading of the pollutant to the system.

The workgroup's suggestion about considering time to steady-state and environmental half-lives, although interesting, does not seem to resolve the problem of metabolism in food webs. The workgroup's suggestion seems reasonable because chemicals with small environmental half-lives rarely produce measurable residues in aquatic organisms. However, even though a chemical is rarely detected in aquatic organisms, this does not necessarily mean that bioaccumulation processes do not occur. It could be that the concentrations of the chemical in the ambient water are so low that the residues in aquatic organisms are not detectable even with the bioaccumulation processes.

Finally, we note that the issue of environmental persistence is most appropriately addressed during the permitting process with the use of dynamic water quality models. Such models can account for degradation processes (e.g., hydrolysis, volatilization, photolysis) in the wasteload allocation and subsequent derivation of the permit limit (U.S. EPA 1991).

Sediment interaction. The workgroup noted that sediment interaction (benthic-pelagic coupling) can be a dominant driver of bioaccumulation and that it should be incorporated in some manner. The FCM methodology does include the benthic-pelagic coupling, as noted by the workgroup. The three sets of FCMs provided in the 1998 draft of the methodology presented FCMs for a purely benthic food web, a mixed benthic-pelagic food web, and a purely pelagic food web. Benthic-pelagic coupling is incorporated via the diet of the consumers in the food web.

Other FCM Comments. The workgroup pointed out that FCMs have some potential problems. First, no one food web can realistically represent the entire United States. However, the workgroup did indicate that a default food web could be used in many cases to provide acceptable estimates. Second, the workgroup suggested that for broad, general application (of the default food web structure), there remain a number of unvalidated assumptions that might be the source of considerable uncertainty (when using the default food web). Uncertainties include: (1) variability in diet, physiology, and ambient conditions; (2) dietary lipid content and its relationship to bioaccumulation and toxicity; and (3) all chemicals and organisms act ideally (i.e., various physical, chemical, and biological modifying factors are identical). The workgroup recommended that additional guidance and limitations be provided on the use of FCMs in criteria development.

The workgroup agreed with EPA that the scientific understanding of aquatic food web processes is known well enough to develop a default food web structure that provides a realistic representation of the processes occurring in aquatic food webs for many ecosystems.

EPA is using state-of-the-art food web models for deriving FCMs, which incorporate the latest thinking and knowledge on the processes occurring in aquatic food webs. The workgroup suggests that the assumptions used in constructing these models are largely unvalidated. We recognize that any modeling formulation of contaminant behavior in aquatic food webs requires simplification of a very complex biological system in order to assemble a tractable model. These simplifications do not imply or mean that our scientific understanding of all processes occurring in food webs is complete. As documented in the scientific literature by Gobas and coworkers, MacKay and coworkers, and Thomann and coworkers (all model-building research groups), these simplifications provide reasonable model formulations with good predictive power.

EPA has performed an analysis of the importance and sensitivities of individual input parameters for food web models and of the overall uncertainties associated with predictions from food web models (Burkhard 1998). We have provided additional discussion in the TSD outlining the results from these analyses and their implications for deriving FCMs. Comparisons between measured and predicted BAFs for the Lake Ontario food web using the Gobas and Thomann food web models resulted in average ratios of 1.2 and 2.5, respectively, for PCBs and chlorinated pesticides. The overall uncertainties (expressed as the ratio of the 90th to 10th percentile values in the distribution of predicted BAFs) associated with the Gobas and Thomann models were a factor of 3.6 and 4.0, respectively, for a chemical with a log K_{OW} of 6.5 for the Lake Ontario food web. The small ratios (of predicted to measured BAFs) and small uncertainties associated with both the Gobas and Thomann food web models strongly suggest that the assumptions used do not introduce large uncertainty into the model predictions as suggested by the workgroup.

We have fully considered the workgroup's comment regarding applicability of the proposed FCMs, and, consistent with our responses to that comment and to the previous one requesting clarity on which FCM to use, we have limited the use of FCMs to nonionic organic chemicals with log K_{OW}s $4.0 in both the national default methodology and the site-specific methodology. In addition, EPA has restricted the use of model-derived FCMs in situations where metabolism has been shown to be important. EPA appreciates the workgroup's concern that not all chemicals have identical behavior.

The workgroup suggested that additional guidance be provided on the uncertainties associated with input parameters such as diet, organism physiology (e.g., weight, temperature preferences, and lipid content), sediment water disequilibrium, lipid content of the diet, and with processes modifying bioaccumulation potential. Because EPA understands that the default food web structure might not be appropriate in some site-specific conditions, the methodology includes procedures for making site-specific modifications to BAFs derived using the national methodology. These procedures allow the use of site-specific parameters in the generation of FCMs. As suggested by the workgroup, EPA has provided additional guidance, information, and clarification on the uncertainties associated with the use of the food web models to

determine FCMs.

> ***Issue 2:*** *Available approaches and data to account for metabolism in the determination of a BAF value, and to predict food chain multipliers.*

Metabolism

The workgroup confirmed EPA's assertion that no reliable, broadly applicable approach exists to predict the metabolic breakdown of organic chemicals by biota, and that this is a significant limitation in the state of the science and affects the proposed methodology. Rather than assume no metabolism for all organic chemicals, the workgroup recommended that EPA develop a chemical grouping scheme and guidance for circumstances in which an assumption of no metabolism is reasonable (e.g., nonplanar PCBs, several chlorinated pesticides) and in which complete loss of a chemical via biotransformation could be assumed (e.g., many aromatic hydrocarbons).

This suggestion is a reasonable idea in theory, but the general lack of metabolism data prevents implementation of such an approach. Data do not exist for either individual chemicals or chemical classes, or for the metabolic abilities of individual organisms. Generally, invertebrate species (e.g., muscles, clams, benthic invertebrates, lobster, shrimp, and crabs) tend to have much lower metabolic abilities than vertebrate species (e.g., fish in aquatic food webs). Although many of the users of these guidance documents are focused on fish as their target species, it is important to note that on average invertebrate aquatic species compose a large portion of the human diet. Such organisms include shrimp, crabs, lobster, scallops, and clams, and most of these organisms have substantially lower metabolic abilities than vertebrate species like fish. Given that these methods are for the protection of human health, EPA cannot ignore the invertebrate species in the determination of bioaccumulation potential for the chemical of interest. In some cases, bioaccumulation potential might be fairly small in fish because of metabolism processes for a chemical, whereas, in contrast, bioaccumulation potential might be very large in invertebrate species because these organisms do not possess the metabolic pathways or have substantially lower metabolic abilities for metabolizing the chemical.

EPA has developed a table to be put in the TSD for chemicals that are not substantially metabolized or are very slowly metabolized. This table in all likelihood contains no false positives (i.e., chemicals that are on the list but are easily metabolized) is not all-inclusive because there are numerous chemicals (e.g., hundreds of thousands in use commercially today) for which few or no metabolism data exist.

We disagree with the workgroup that a table of completely metabolized chemicals can be developed. This belief is based on the lack of whole-organism metabolic rate data for fish and other aquatic species, the lack of metabolic rate databases of any type for any species, and the general inability to extrapolate from *in vitro* studies using liver microsomes, cells, or organ slices to whole organism rate constants. In addition, predictions from QSAR relationships based on *in vitro* data have extremely large uncertainties. The following example for PAHs, which are suggested by the reviewers as being completely metabolized in vertebrate species, illustrates the

difficulties in developing a table of completely metabolized chemicals. Burkhard and Lukasewycz (2000) reported log of field-derived BAFs on a freely dissolved and lipid normalized basis versus the log of the octanol-water partition coefficient (K_{OW}) for phenanthrene, fluoranthene, pyrene, benz[a]anthracene, and chrysene/triphenylene in lake trout. Their data showed that bioaccumulation did occur for all five PAHs because all of the log BAFs were greater than zero, even though the concentrations in the fish were very low (i.e., 0.06 to 2.9 ppb). If no metabolism occurred, the log BAF should be equal to the chemical's log K_{OW} (ignoring biomagnification processes). The ratios of the field-measured log BAFs to log K_{OW}s ranged from 0.2% to 34%, suggesting that some metabolism did occur. Pyrene's log BAF was 34% of its log K_{OW}, suggesting that partial metabolism but not complete metabolism occurred for this chemical. This example highlights the difficulties faced in constructing a table for completely metabolized chemicals, because even for a class of chemicals believed to be completely metabolized, field data suggest otherwise. If the completely metabolized table were limited to only those chemicals with known metabolic data, this table would in all likelihood contain very few entries. If we were to use expert opinion, advice, or best scientific judgment, we believe that numerous false positives would be present because of the lack of data; that is, chemicals that are not completely metabolized and would likely not be defensible from a public health protection perspective. In view of these difficulties, EPA does not agree with the workgroup's suggestion of developing a table of completely metabolized chemicals.

The workgroup suggested that an alternate methodology that relied on chemical-specific or species/trophic level-specific elimination rates might be used for addressing metabolism. However, it was acknowledged that this approach would be resource-intensive and that much of the information would be direct measures of organism-level metabolic rates (e.g., enzyme induction, metabolite structures). The workgroup suggested that such an approach might be used to screen or prioritize chemicals most appropriate for AWQC derivation using the current methodology.

The workgroup suggested that research initiatives on the extrapolation of organism-level metabolic rates to whole organism rates and species to species extrapolations (e.g., from rats to fish) be initiated. In the future, once a sufficient body of knowledge from such efforts becomes available, EPA will consider revising these guidance documents to include the results of the investigations.

We disagree with the workgroup's suggestion that using direct measures of organisms' metabolic rate to evaluate bioaccumulation potential for screening or prioritizing chemicals for AQWC derivation is practical now or advisable. EPA will continue to use the risk-based approach for selecting chemicals to derive AWQC, rather than just relying on bioaccumulation potential, because other factors can contribute to potentially significant health risks for individual chemicals.

> **Issue 3:** *Any other available models that EPA should consider for inclusion in the revised methodology for estimating bioaccumulation.*

> Alternative Models

The alternative models available for assessing bioaccumulation were judged by the workgroup to all have similar structure, assumptions, and limitations. The differences were not thought to be important on a national scale, but might be for a specific site. The workgroup thought that additional modifications could be made to address some of the model assumptions (e.g., sediment disequilibrium, metabolism) in addition to the use of isotopes for empirically modeling residues.

We agree with the workgroup that there is a general lack of alternative models that differ in their structure and assumptions for estimating bioaccumulation. In the revised guidance, we have allowed appropriately validated alternative models to be used on a site-specific basis. EPA notes that the proposed model and other available models include explicit consideration of sediment-water disequilibrium and include the capability to account for metabolism of the chemical by the inclusion of the first-order, whole organism metabolism rate constants, k_m. When no metabolism is assumed, k_m is set equal to zero.

The workgroup suggested that use of stable isotopes for nitrogen and carbon (e.g., $^{*15}N$ or $^{*13}C$) might be useful in modeling chemical residues. EPA does not believe that $^{*15}N$ or $^{*13}C$ signatures can be used to predict chemical residues in a given ecosystem for a given organism, because chemical residues in fish and other aquatic organisms are a function of the chemical loading to the ecosystem from past and current practices. However, as demonstrated by Cabana and Rasmussen (1994) using mercury and Canadian shield lakes, it may be feasible to perform this prediction with a reasonable degree of accuracy for ecosystems of similar nature and loading patterns, assuming a predictive relationship can be developed for other chemicals.

EPA believes that $^{*15}N$ or $^{*13}C$ signatures are extremely useful in establishing food chain length, trophic levels status of individual organisms, and food web structure or function for specific ecosystems. Traditional methodologies for determining these characteristics in aquatic food webs such as visual observation, gut analysis, and professional interpretation of expected feeding interactions are all very difficult and have high uncertainties. In addition, $^{*15}N$ or $^{*13}C$ signatures provide a time course integration of dietary consumption patterns, whereas traditional methodologies (e.g., gut analysis) represent dietary consumption patterns for single moments in the organism's life. In the past, if food web structure was not known, a linear food web structure was assumed in modeling effects (e.g., Thomann 1989). However, in more recent modeling efforts, Morrison et al. (1997) used food web structures that represent actual dietary consumption patterns. $^{*15}N$ or $^{*13}C$ signatures allow one to determine trophic level status of organisms on a continuous scale rather than the lumping of organisms into general categories as previously done, that is, trophic levels 1, 2, 3, or 4. Numerous investigators, including Bromann et al. (1992), Cabanna and Rasmussen (1994), Kiriluk et al. (1995), Kucklick et al. (1996), and Kidd et al. (1998), have demonstrated that $^{*15}N$ signatures are well correlated with biomagnification of PCBs, DDE, PCDD/Fs, and mercury in specific aquatic food webs. Their results suggest that stable isotope data of nitrogen may be useful in estimating biomagnification factors for nonmetabolizable hydrophobic chemicals such as PCBs and DDE.

Minigawa and Wada (1984) have reported that 3.4‰ enrichment of $^{*15}N$ should be expected on average for a predator consuming a prey with a constant $^{*15}N$ signature. Vander Zanden

and Rasmussen (1996) reported that omnivory feeding behavior often causes differences in the $*^{15}N$ signatures to be smaller than 3.4‰ between lake trout and their primary prey, forage fish. Vander Zanden and Rasmussen (1996), when calculating BMFs for a full trophic level (i.e., +3.4‰ enrichment of $*^{15}N$) observed much larger BMF estimates than those ignoring omnivory behavior. EPA believes that $*^{15}N$ or $*^{13}C$ signatures will, in all likelihood, be a very useful tool for estimating BMFs for nonmetabolizable hydrophobic chemicals in the future. The scientific underpinnings of this tool are under active research and until further developments are made, we believe that using this tool for determining BMFs for use in the derivation of national AWQC would be premature.

Issue 4: Whether the draft BAF methodology is an improvement over the 1980 methodology and, in particular, whether it is likely to be more predictive of bioaccumulation.

1980 Versus 1998 draft Methodology

The workgroup stated that the 1998 draft methodology is a theoretical improvement over the 1980 methodology and is more predictive for the chemicals and sites referenced in the TSD. However, the workgroup said that it is not known whether the 1998 draft methodology is more predictive than the 1980 methodology for other chemicals and sites and that further verification and comparisons are needed to address this issue. The workgroup also commented that the 1998 draft methodology requires many assumptions and measurements and, as proposed in its current form (1998), contains an aggregate uncertainty that is too high for broad regulatory application.

We agree with the reviewers that the draft 1998 methodology represents a theoretical improvement over the 1980 methodology because it emphasizes a more explicit and systematic assessment of bioaccumulation (i.e., chemical accumulation from water, diet, sediment) compared with the 1980 methodology, which emphasizes the assessment of bioconcentration (i.e., uptake from water only). [It should be noted that the 1980 AWQC Guidelines do allow for the use of "field-BCFs" (currently termed field-BAFs) when such values are substantially higher or lower than laboratory-measured or K_{OW}-estimated BCFs. Guidance on the use of "field BCFs" is very limited in the 1980 guidelines.] EPA notes that consideration of dietary and other sources in addition to water has been shown to be very important for many persistent, highly bioaccumulative pollutants of concern (e.g., Russell et al. 1999; Burkhard et al. 1997; Oliver and Niimi 1983, 1988; Niimi 1985; Swackhamer and Hites 1988; Watras and Bloom 1992; U.S. EPA 1997). We recognize that evaluation of various aspects of the draft 1998 methodology (such as predicted BAFs using K_{OW}, food chain multipliers, and BSAFs) has focused on persistent, hydrophobic organic chemicals including PCBs, chlorinated pesticides, PCDDs, and PCDFs in relatively few (but diverse) ecosystems. These systems include the hydrodynamically complex and tidally influenced area of Bayou d'Inde, Louisiana; the more stable, oligotrophic system of Lake Ontario; and by comparison to Lake Ontario, the more shallow, eutrophic system of Green Bay, Lake Michigan. The primary reason for this focus is the limited availability of high-quality field data on bioaccumulation from which to draw such comparisons. Such high-quality field data include studies that measure contaminants in water, sediment, and the food web

over appropriate time scales in addition to other measurements such as organic carbon and lipid fraction. We also note that other aspects of the methodology (e.g., K_{OW}-based estimates of bioconcentration factors) have been tested extensively in the scientific literature for numerous organic chemicals (Vieth et al. 1979; Oliver and Niimi 1983; Mackay 1982; Chiou 1985; and others) and have been used in developing AWQC for nearly two decades. Nevertheless, we agree that additional testing of various aspects of the methodology is desirable and have provided further evaluation of the national BAF methodology using two data sets (Fox River and Hudson River). We believe that these sites are appropriate for additional comparisons because they represent lotic systems that would likely differ in their ecological and hydrological characteristics compared with the sites already examined.

Regarding the uncertainty in the draft 1998 bioaccumulation methodology, we have made extensive revisions to the methodology that we believe address many of the workgroup's concerns and reduce overall uncertainty in BAF estimates. These changes include the following: (1) development of separate procedures for deriving BAFs for different chemical classes (e.g., high versus low hydrophobicity, high versus low metabolism in biota, ionic versus nonionic organics); (2) simplification of procedures for organic chemicals with low hydrophobicity; (3) recommending that K_{OW}-based estimates of BAFs and food chain multipliers not be used for nonionic organics that are known to metabolize substantially in targeted biota (e.g., benz[a]pyrene in fish); and (4) restricting the use of the BSAF methodology. It should be noted that many of the uncertainties raised by the workgroup are also present in the 1980 methodology, which is oriented toward assessment of bioconcentration factors using lab-BCFs *and* K_{OW}-based predictions. Furthermore, in the 1980 guidance no explicit guidance exists on modifying the national default BCFs for site- or region-specific concerns. Therefore, we believe that the revised 1998 bioaccumulation methodology represents a substantial improvement over the 1980 methodology for assessing bioaccumulation for deriving AWQC.

The workgroup commented that the uncertainties in the 1998 draft methodology would likely overestimate the BAF but were not certain by how much. We agree with the workgroup that some of the procedures of the 1998 draft methodology (e.g., K_{OW} and FCM-predicted BAFs) might lead to overestimates of BAFs for certain types of pollutants, such as those that are metabolized substantially to chemical forms not addressed by the AWQC. However, we disagree with the comment that implies that, in general, EPA's draft methodology would lead to across-the-board overprediction of BAFs. Field BAFs, the first tier in the data preference hierarchy, represent direct measures of bioaccumulation. We are not aware of any reason why the treatment of uncertainty or variability in such field BAF estimates would consistently lead to across-the-board overestimates of bioaccumulation, regardless of the pollutant type, since such values are based on central tendency estimates within and across species of a given trophic level. Similarly, the calculation of freely dissolved concentration for nonionic organic chemicals using the three-phased partitioning model is based on central tendency estimates of input parameters. We also know of no reason why the treatment of uncertainty and variability in laboratory-measured BCFs would result in consistent overestimates of BAFs. For highly hydrophobic contaminants that do not metabolize substantially in tissues, use of the BSAF-predicted and $K_{OW} \times$ FCM-predicted BAFs also does not appear to be biased toward overestimating field-measured BAFs. This is demonstrated by comparisons made in the TSD (Exhibits 2.4.1, 2.4.3,

and 2.4.6) for BSAFs and those made by Burkhard et al. (1997) for the $K_{OW} \times$ FCM method (Figure 2).

The workgroup questioned how AWQC will (or could) be linked to sediment quality criteria (SQC) and inquired whether there will be SQC for the protection of human health. EPA agrees that sediments can serve as important sinks and sources for waterborne contaminants, which if not considered can lead to unacceptable ecological and human health risks. EPA is nearing completion of the first equilibrium-partitioning sediment guidelines (ESGs) for PAH mixtures, cationic metals, and dieldrin/endrin and expects to publish these guidelines in late spring of 2000. EPA notes that the partitioning theory of nonionic organic chemicals used to calculate ESGs is the same as that used in EPA's draft bioaccumulation methodology, which helps to ensure consistency in the two approaches. It should be noted that to the extent that contaminated sediments are contributing to bioaccumulation in aquatic food webs, the draft (and subsequently revised) procedures for measuring BAFs and BSAFs in the field do account for this exposure at the sites from which the BAFs and BSAFs are measured. Finally, although we are not currently planning to develop human health AWQC that are solely based on sediment concentrations, we are in the early stages of conceptualizing environmental criteria that integrate exposure from multiple sources, including sediments. These integrated criteria would also evaluate risks to multiple receptors (aquatic life, wildlife, human health) simultaneously. Thus, EPA's desire is to develop future criteria that are truly comprehensive in their exposure and receptor evaluations and rely on a consistent set of methodologies that reflect the current state of the science.

2. Response to Issues for Public Comment Listed in the Federal Register (7.2)

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

Tiered Hierarchy

The workgroup considered the hierarchy to be acceptable for a site-specific analysis (given more explicit guidance), but not for use on a national level as was originally proposed. They further recommended that EPA make clear that although the national BAF can be derived based on a reliable field-measured BAFs with limited regional coverage, site-specific studies are allowed if the national BAF appears to not be representative of that site.

As we discussed in our responses in Section 1 above, we have made substantial changes to the 1998 draft methodology in regard to general concerns about using BAFs, document readability and scale of application, and the 1980 versus new methodology, which we believe addresses many of the peer reviewers' concerns and resulted in an improved methodology for assessing bioaccumulation that can be implemented effectively throughout the United States. The revisions include improvements in the readability and clarity of the guidance, such as separating EPA's guidelines for deriving national BAFs from its guidelines for deriving site- or region-specific BAFs. We have also simplified parts of the draft methodology for certain types of pollutants where the benefits of the added complexity (i.e., improved accuracy) are not likely be realized. For example, for nonionic organic chemicals of low hydrophobicity, the methodology has been

revised to give equal consideration to the use of laboratory-measured BCFs and field-measured BAFs since the benefits of field-measured BAFs over laboratory-measured BCFs would likely be marginal. For the same reason, the requirement to derive separate, trophic level–specific BAFs for low K_{OW} chemicals has been relaxed. Changes were also made to address the workgroup's concerns about uncertainty in certain key areas, such as placing restrictions on the use of K_{OW}- and BSAF-predicted BAFs for certain types of pollutants.

Regarding the use of site-specific studies to modify national BAFs, EPA emphasized in the 1998 draft methodology, and will continue to encourage, that such studies are appropriate and recommended in situations where there are concerns about the representativeness of a national BAF. We are developing detailed procedures for designing and conducting field BAF studies, which are scheduled for completion within the year following the publication of the revised AWQC methodology. The guidance for conducting field BAF studies addresses differing chemical properties of the pollutant (e.g., K_{OW}) and site characteristics that can impact uncertainty in BAF measurements. We recognize (and have made clear in the revised methodology) that because of current limitations in availability of high-quality field studies, some national BAF values might be based on results from a few field studies, which might represent to varying degrees different sites around the United States. However, EPA notes that although such national BAFs may be directly supported by a few studies, indirect support (and greater confidence) can be derived by comparing the results of BAF estimates using other tiers of the methodology (e.g., BSAF, laboratory-measured BCFs, $K_{OW} \times$ FCM-predicted BAFs). Thus, in some cases, a field-measured BAF may be supported by multiple lines of evidence. In other cases, uncertainties in a field-measured BAF may outweigh its preference to BAFs derived from the lower tiers. We have provided additional text to better emphasize the assessment of uncertainty in field-measured BAFs (and BAFs derived using other tiers) when deriving national BAFs.

Finally, regarding limiting the guidance to site-specific application, EPA notes that the current 304(a) AWQC have been implemented on a national scale for nearly two decades. As discussed under Section 1, Issue 1, in our response to the workgroup's comments on default lipid values, we believe that restricting the bioaccumulation methodology only to the development of site-specific BAFs would greatly hinder the implementation of water quality criteria throughout the United States. We believe this would be the case because many States, Territories, and authorized Tribes lack the resources to develop site-specific BAFs for all of their pollutants of concern and subsequent adoption of AWQC would be delayed substantially.

Although the BSAF approach may be reasonable for the chemicals examined in the TSD, the workgroup thought that it was not reliable for all chemicals and that it should be dropped from the proposed hierarchy. Specifically, the workgroup made the following comments: (1) the BSAF approach ignores differences in gut assimilation efficiency, metabolism, and bioavailability from sediment; (2) BSAFs have not been widely validated for general use with organic chemicals; and (3) the relative contribution of food and water routes to the BSAF vary with K_{OW}.

EPA believes that the BSAF method for determination of BAFs is valid and is needed for

chemicals with nondetectable or difficult-to-predict concentrations in water. We agree that the BSAF method should not be used for all organic chemicals that may be addressed through the human health methodology. Although proper choice of reference chemicals to match properties of less hydrophobic target chemicals should allow the BSAF method to work for a wider range of chemicals, EPA has restricted application of the method to the following: (1) chemicals that, because of their chemical properties, cannot be measured or are very difficult to measure in water; and (2) chemicals that perhaps could be measured but have not been, yet need an assessment of bioaccumulation. We have also provided more specific guidance on selection of reference chemicals and use of multiple reference chemicals to secure the most accurate estimate of a chemical's BAF.

We do not agree that the BSAF method ignores differences between chemicals in their gut assimilation efficiency, metabolism, and bioavailability from sediment. The ability to measure these differences through BSAFs for chemicals without directly measurable BAFs is precisely why the BSAF method was proposed. Gut assimilation efficiencies for nonionic organic chemicals with log K_{OW}s $\$$ 4.0 are uniformly above 80% (e.g., Nichols et al., 1998). The cumulative effects of metabolism of the chemical in the food chain on the chemical concentration in the organism are incorporated in the BSAF in the same manner as in a measured BAF (same numerator). Bioavailability differences between organic chemicals are a function of their log K_{OW}s and are most important for log K_{OW}s $\$$ 4.0. Based on the critical condition that J_{socw}/K_{OW} for both chemicals are similar, the BSAF method has been shown to accurately predict BAFs in two different Great Lakes ecosystems. The factor J_{socw} is a ratio that represents the disequilibrium between the concentration of a chemical in sediment (normalized for organic carbon content) and water. However, EPA agrees that the BSAF method could be bolstered with further validation. Thus, we have added more validation in the revised TSD using new data sets that meet the water, surface sediment, and biota sampling and analysis requirements.

We agree that relative contributions of food, water, and sediment routes of exposure to BSAFs (and BAFs) vary with K_{OW}. Although a BSAF indexes the concentration of a chemical in fish to concentration in sediment, rather than water as for the BAF, both have a common numerator that measures the sum of all routes of exposure. Thus, both BSAFs and BAFs vary with K_{OW}, depending on the relative contribution of food, water, and sediment, and the BSAF method accounts for this variation in the same way that measured BAFs do.

The workgroup noted that "for the chemicals examined (persistent and bioaccumulative), extrapolation to other circumstances may be reasonable." We believe that restricting the use of the BSAF method to highly hydrophobic chemicals difficult to measure in water, clarifying the use of reference chemicals, elaborating on the primacy of the sediment-water fugacity equivalence condition for use of the method, and validation with additional data sets have alleviated the workgroup's concerns about use of this new method. Finally, it should be noted that use of the BSAF method, by incorporating the chemical-specific effects of bioavailability and metabolism into the BAF estimate, will allow measurement of BAFs that are significantly less than those predicted from a BCF, a K_{OW} with a food chain multiplier, or a food web model that assumes no metabolism.

The workgroup commented that it is unclear whether it is EPA's intent to take the geometric mean of the geometric mean species BAFs for calculating the trophic-level BAF or if this calculation is correct. The goal of EPA's national 304(a) AWQC is to be protective of public health generally. Accordingly, EPA's national 304(a) AWQC values are derived with parameter estimates for dose-response assessment that are upper bounds in exposure assessment parameter estimates using a combination of mean values (e.g., body weights, non-fish dietary intakes) and upper percentile values (e.g., drinking water and fish consumption rates) to provide an overall high-end (conservative) public health risk estimate. EPA determines its estimates of the BAF on central tendency estimates. When variability in BAFs occurs within or across species of a trophic level, it is EPA's intent to express the species-mean BAF as the geometric mean of acceptable species BAF values. Likewise, it is EPA's intent to express the trophic-level mean BAF as the geometric mean of the species-mean BAF values. Given the limited data typically available for field-measured BAFs and laboratory-measured BCFs, we believe that this procedure is appropriate. We recognize that ideally, one would want to weight each species-mean BAF by the extent to which that species represents the likely dietary exposure of the target population. However, as described on pages 239-256 of the 1998 TSD, consumption rate information is not available on a national scale at the individual species level. Therefore, each species-mean BAF value is weighted equally within a trophic level for the purposes of deriving a trophic level mean BAF.

After reviewing this issue further, we believe that States, Territories, and authorized Tribes may wish to weigh the contribution of one species' BAF to a greater or lesser extent than a BAF for another species based on State or site-specific data. Therefore, in the guidelines for developing site- or region-specific BAFs, we have provided additional guidance on this issue.

> **Issue 2:** *Is the procedure for estimating the consumption-weighted 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?*

National Default Lipid Value

The workgroup considered the procedure used to derive the national default value as reasonable but cited concerns expressed earlier (see Section 1, Issue 1, "Default Lipid Value"). EPA's response to these concerns appears under Section 1, Issue 1, "Default Lipid Value."

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

Freely Dissolved Fraction Equation

The general approach chosen by EPA to estimate the freely dissolved fraction of a chemical was considered by the workgroup to be the most appropriate one. However, the workgroup stated

that EPA needs to make modifications to these equations and provide a more explicit description of the underlying assumptions and potential magnitude of associated error as discussed above in Section 1, Issue 1, "Freely Dissolved Fraction." EPA's response to this comment appears above in Section 1, Issue 1, under "Freely Dissolved Fraction."

Issue 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?

Default DOC and POC Values

The workgroup considered the national defaults as appearing to provide valid mean values of dissolved organic carbon (DOC) and particulate organic carbon (POC). However, the workgroup made several suggestions to expand on these values: (1) provide a measure of variability around the means (e.g., confidence limits); (2) provide more detailed data in an appendix or separate document (including State-specific values); (3) provide additional guidance on the potential for high spatial and temporal variability in DOC and POC; and (4) provide appropriate analytical methodologies for measuring DOC and POC.

We agree with the workgroup that the national default values for DOC and POC described in the 1998 draft methodology provide reasonable estimates of mean values. Although in the 1998 draft TSD we provided some measure of variability around these mean estimates (e.g., standard deviation) both across and within water-body types, we agree with the reviewers that a more thorough characterization of variability in organic carbon values would be desirable. In the revised 1998 draft methodology, the analysis of DOC and POC data to has been expanded to include other measures of variability (e.g., percentiles, confidence limits) and provide a breakdown of estimates by State and where data allow, by water-body type within a State. EPA has also decided to made the DOC and POC database available to States, Territories, and authorized Tribes for use in modifying national default estimates on a State/Tribal or local basis. A more complete characterization of the DOC and POC database has been provided in BAF TSD. Additional guidance will also be provided in the forthcoming bioaccumulation field plan document on measuring DOC and POC, including the selection of analytical methodologies and addressing temporal and spatial variability.

Issue 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?

Metabolism

See EPA's response to this issue above under Section 1, Issue 2, "Metabolism."

Issue 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?

<u>Models and FCMs</u>

The workgroup did not offer other models for EPA's consideration but did comment that flexibility is necessary in the selection of model parameters to enable site-specific adjustments to be made. They further noted that guidance on doing this is lacking in the proposed methodology and lacking in general, thus making the development of science-based guidance on FCMs difficult and their application on a national scale potentially inappropriate. The workgroup recommended the generation of additional data to refine and validate food web models, including the use of isotopic studies for analyzing food web structures.

As we discussed earlier, in Section 1, Issue 1, under "Food Chain Multipliers," we strongly recommend wherever possible that site-specific FCMs be determined using site-specific food web parameters. The revised site-specific guidance TSD provides guidance on how one should assess the diets, lipid contents, and weights of organisms composing the food web, and important environmental parameters (e.g., sediment water column disequilibrium) used in calculating FCMs. Guidance has also been provided for calculating the FCMs in the revised site-specific portion of the TSD.

As we discussed earlier, in Section 1, Issue 3, "Alternative Models," we believe nitrogen and carbon isotopic signatures (i.e., $^*{}^{15}N$ or $^*{}^{13}C$) are extremely useful for establishing food web structures and trophic levels of individual organisms. However, EPA believes the science supporting the use of $^*{}^{15}N$ or $^*{}^{13}C$ signatures is still developing and not ready for use in a regulatory program. Isotopic signatures may be a very useful tool for estimating BMFs for nonmetabolizable hydrophobic chemicals in the future when the scientific underpinnings of this tool are further clarified.

Consideration of the Electric Power Research Institute (EPRI) mercury food chain model was recommended by the workgroup. EPA is currently in the process of revising its ambient human health criteria for methylmercury. As part of this process, EPA may consider the use of the EPRI methylmercury bioaccumulation model and other models for use in estimating mercury bioaccumulation. Currently, these models have the greatest appeal for use on a site-specific basis.

> **Issue 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 the most appropriate?*

<u>Selecting K_{OW} Values</u>

The second (more detailed) option for selecting the K_{OW} value was preferred by the workgroup, although they cautioned that the molecular fragment method should be used as a last resort. Additionally, the workgroup thought that a general consensus on K_{OW} values already exists in the scientific community (e.g., Mackay et al. 1999) and that EPA should simply publish a list of

recommended values.

The second method for selecting the K_{OW} values has been retained in the revised methodology because EPA believes that it provides more complete guidance on selecting K_{OW} values for use in AWQC derivation. EPA further agrees that it is desirable to publish a list of K_{OW} values that have been selected using the K_{OW} selection methodology. We plan to publish a list of such chemicals following issuance of our revised AWQC methodology.

We agree with the cautionary note by the workgroup about the molecular fragment method. The K_{OW} selection protocol uses a weight-of-evidence approach, where "assigning a K_{OW} . . . will necessarily involve scientific judgment in evaluating not only the reliability of all data inputs but also the accretion/concretion of evidence in support of the recommended K_{OW} value." The molecular fragment method is included in the K_{OW} selection protocol for circumstances where disagreement exists among K_{OW} estimation methods (e.g., ClogP, LOGKOW, and SPARC K_{OW} estimation computer programs), when K_{OW} measurements differ substantially from predictions using the K_{OW} estimation methods, and when an absence or scarcity of reliable data exists. One good example of possible use of the molecular fragment method is for the chemical photomirex, for which K_{OW} estimation methods disagree and no measurements have been made. Using the molecular fragment method with mirex, an estimate can be derived for photomirex. This estimate then provides additional information to be used in the selection of the recommended K_{OW} value.

> ***Issue 8:*** *Should properly derived field-measured FCMs take precedence [over] FCMs derived using the Gobas (1993) model?*

Field-Based FCMs

In general, the workgroup preferred the use of field-measured FCMs over model-derived FCMs. However, they emphasized that proper evaluation of these two approaches would require a more complete comparison and encouraged EPA to perform such an analysis. EPA agrees that in theory, use of field-measured FCMs would be preferred to the use of model-derived FCMs (which assume no metabolism), particularly for contaminants where metabolism is of concern. Field-derived FCMs reflect any metabolism that occurred in the food web. However, EPA believes that effective use of field-derived FCMs requires knowledge of the food web structure at the site(s) from which they are obtained in order to derive valid FCMs. More detailed guidance has been added to the revised methodology on the use of field-derived FCMs.

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