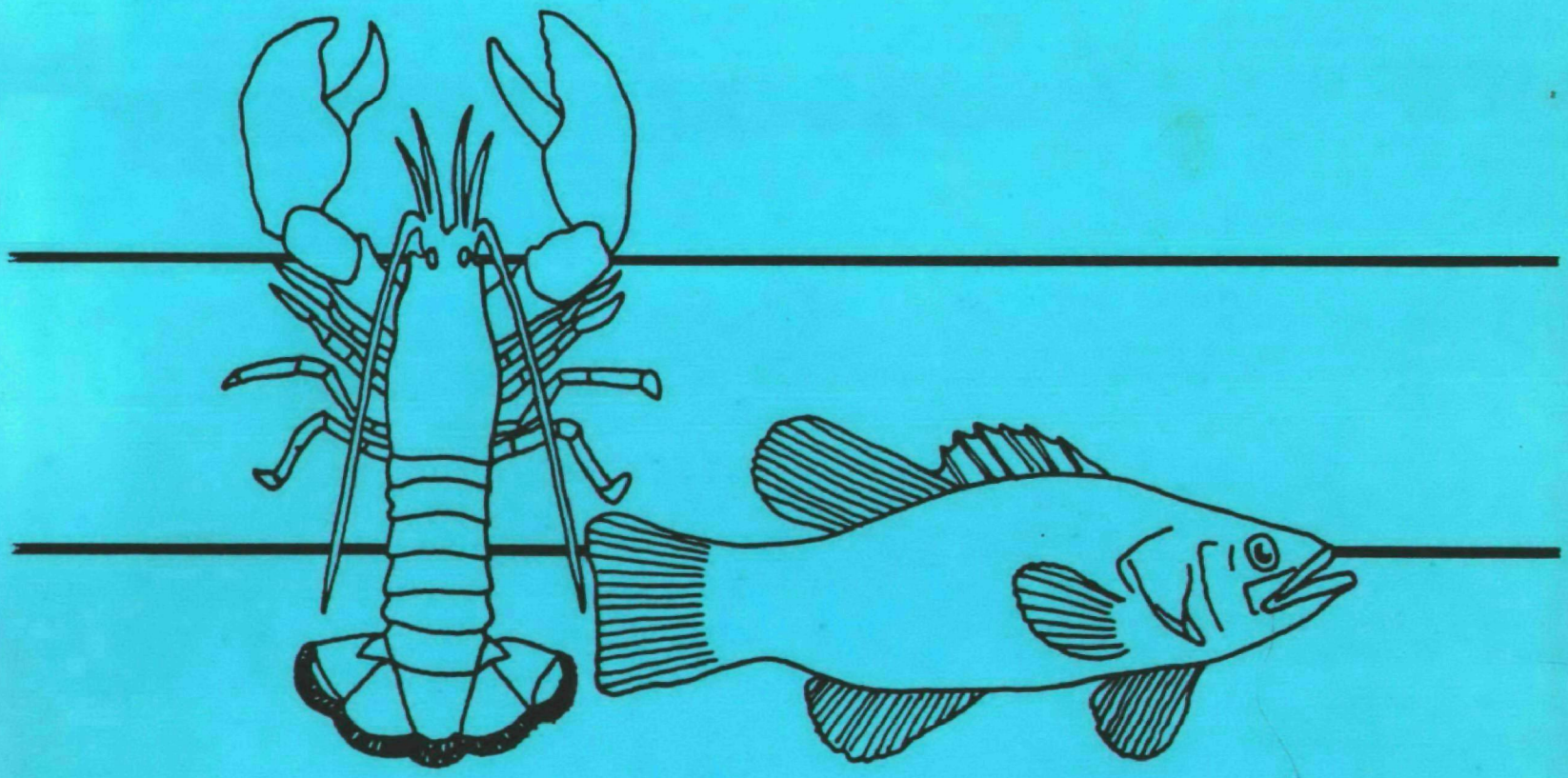
United States
Environmental Protection
Agency

Office of Water Regulations
and Standards
Washington, DC 20460

EPA

Water Quality Criteria Methodology



FINAL REPORT

on

WATER QUALITY CRITERIA METHODOLOGY

to

U.S. ENVIRONMENTAL PROTECTION AGENCY
Criteria and Standards Division

August 6, 1990

Contract No. 68-03-3534
Work Assignment No. H2-52

BATTELLE
Washington Environmental Program Office
2101 Wilson Boulevard, Suite 800
Arlington, Virginia 22201

Revised October 22, 1990

1.0 BACKGROUND

EPA's water quality criteria are developed under the authority of Section 304(a)(1) of the Clean Water Act which reads as follows:

> "The [EPA] Administrator, after consultation with appropriate Federal and State agencies and other interested persons shall develop and publish, within one year after the date of enactment of this title (and from time to time thereafter revise) criteria for water quality accurately reflecting the latest scientific knowledge (A) on the kind and extent of all identifiable effects on health and welfare including but not limited to, plankton, fish, shellfish, wildlife, plant life, shorelines, beaches, esthetics, and recreation which may be expected from the presence of pollutants in any body of water, including ground water; (B) on the concentration and dispersal of pollutants, or their by products, through biological, physical, and chemical processes; and (C) on the effects of pollutants on biological community diversity, productivity, and stability, including information on the factors affecting rates of eutrophication and rates of organic and inorganic sedimentation for varying types of receiving waters."

The Section 304(a)(1) requirement for development of criteria supports the goal of fishable swimmable waters given in Section 101(a)(2) which states that:

> "it is the national goal that, wherever attainable, an interim goal of water quality which provides for the protection and propagation of fish, shellfish, and wildlife and provides for recreation in and on the water be achieved by July 1, 1983."

The Section 304(a)(1) water quality criteria are issued as guidance to the States. These criteria are not enforceable regulations. Rather, these criteria present scientific data and provide guidance on the environmental effects of pollutants which can be useful in deriving regulatory requirements based on consideration of water quality impacts. Under the Clean Water Act, these regulatory requirements may include the promulgation of water quality-based effluent limitations under Section 302, water quality standards under Section 303, or toxic pollutant effluent standards under Section 307. The States are responsible for developing State standards. States may simply adopt EPA's criteria, modify them on a site-specific basis (i.e., develop site-specific criteria), or use an entirely different number, provided that the new number is

scientifically defensible. State standards are submitted to EPA for approval, and if EPA disapproves, either the State must promulgate a new standard, or in rare cases, EPA may promulgate standards for the State if the State fails to develop acceptable standards in a timely manner. For example, prompted by the 1987 CWA, EPA is currently promulgating State toxics standards for certain States which have not done so.

EPA issues both criteria to protect aquatic life and criteria to protect human health. This document confines itself to the methodology for developing criteria to protect human health. The methodology described in this document was published in the Federal Register on November 28, 1980, "Water Quality Criteria Documents; Availability, Appendix C - Guidelines and Methodology Used in the Preparation of Health Effect Assessment Chapters of the Consent Decree Water Criteria Documents" (45 FR 79347). This methodology has been reviewed and approved by EPA's Science Advisory Board. A copy of these guidelines is included in Appendix A of this document.

The purpose of human health criteria is to estimate the ambient water concentration of a pollutant which does not represent a significant risk to the public. Ambient water quality criteria for human health are primarily based on two types of biological endpoints: (1) carcinogenicity and (2) toxicity (i.e., all adverse effects other than cancer). Also, criteria may in some cases be based on organoleptic effects (thresholds for taste or odor). There are essentially two procedures for assessing health effects; one which addresses carcinogens and one which addresses non-carcinogens. The reason for having two methodologies is that, for the purpose of deriving ambient water quality criteria, carcinogenicity is regarded as a non-threshold phenomenon, whereas toxicity is regarded as having a threshold below which there will not be an effect.

Under the assumption that carcinogenicity is a "non-threshold phenomenon," there are no "safe" or "no effect" levels, because even extremely small doses are assumed to elicit a finite increase in the incidence of the response. Therefore, water

quality criteria for carcinogens are presented as a range of pollutant concentrations associated with corresponding incremental increases in the risk of developing cancer.

For compounds which do not manifest any apparent carcinogenic effect, the assumption used to derive a criterion is that the compound has a threshold below which no effects will be observed. This assumption is based on the premise that a physiological reserve capacity (or defense mechanism) exists within the organism which is thought to be depleted before clinical disease ensues. Alternatively, it may be assumed that the rate of damage will be insignificant over the lifespan of the organism. Thus, ambient water quality criteria are also derived for non-carcinogenic chemicals, and presumably result in no-observable-adverse-effect levels (NOAELs) in human populations.

In some instances, criteria are based on organoleptic characteristics, i.e., thresholds for taste or odor. Such criteria are established when insufficient information is available on toxicologic effects, or when the estimate of the organoleptic effect level of the pollutant in ambient water is lower than the level calculated from toxicologic data. It should be recognized that criteria based solely on organoleptic effects do not necessarily represent approximations of acceptable risk levels for human health. Development of these criteria will not be discussed further in this document.

This document describes the methodology used to develop human health criteria for both carcinogens and non-carcinogens. The methodology used includes four steps: hazard identification, dose-response assessment, exposure assessment, and a risk management decision. Each of these steps will be discussed in a separate section below. The criteria developed from this methodology are published in criteria documents for each of the compounds or groups of compounds evaluated. These criteria documents provide the scientific base used to support development of the criteria. As discussed in more detail below, the methodology was not developed to assess fish contamination directly, but can be utilized for this purpose. One goal of this document is to discuss the methodology in detail so that an informed decision can be made concerning its utility for this purpose.

2.0 HAZARD IDENTIFICATION

Hazard identification involves gathering and evaluating data on the types of health injury or disease that may be produced by a chemical, and data on the conditions of exposure under which injury or disease may be produced. It may also involve characterization of the behavior of a chemical within the body and the interactions it undergoes with organs, cells or even part of cells. Data of the latter types may be of value in answering the ultimate question of whether the forms of toxicity known to be produced by a substance in one population group or in experimental settings are also likely to be produced in humans. Hazard identification is not risk assessment; rather it is simply the process of determining whether exposure to an agent can cause an increase in the incidence of an adverse health effect. It includes an associated characterization of the nature and strength of the evidence of causation.

Information for hazard identification can be obtained from EPA's approved toxicology data source, the Integrated Risk Information System (IRIS). IRIS is an electronic data base containing health risk and EPA regulatory information on specific chemicals. It was developed for EPA staff in response to a growing demand for consistent risk information on chemical substances for use in decision-making and regulatory activities. The heart of the IRIS system is its collection of computer files covering individual chemicals. IRIS can be accessed to obtain summaries of key toxicological data to be used in hazard identification.

The results of the hazard identification process influence the nature and the extent of subsequent steps in risk analysis. For example, the endpoint of concern in a dose-response assessment may be selected based on the most severe adverse effect identified in the hazard identification.

In the hazard assessment, an attempt is made to include the known relevant hazard information. The relevant hazard information for a particular compound is summarized in the criteria document prepared to support the derivation of the criteria for that compound. Review articles and reports are often used in the process of data

evaluation and synthesis. Scientific judgement is exercised in the review and evaluation of the data and in the identification of the adverse effects for which protective criteria are developed. The criteria documents are peer reviewed by a committee of scientists familiar with the specific compound(s). These work groups evaluate the quality of the available data, the completeness of the data summary, and the validity of the derived criterion. As noted below, EPA is not developing any new human health criteria at the present time.

In the analysis and organization of the data an attempt is made to be consistent with respect to the format and the application of acceptable scientific principles. Evaluation procedures used in the hazard identification process follow the principles outlined by the National Academy of Sciences in "Drinking Water and Health" (1977), and the guidelines of the Carcinogen Assessment Group of the U.S. EPA.

Chemicals for which human health criteria have been published by EPA include most of the 126 toxic priority pollutants listed under Section 307(a) of the Clean Water Act (see Table 1). The method used in developing the priority pollutant list is unclear; however, toxicity and production were considered in the selection process. EPA has not issued any new human health criteria since 1984, but will issue new ones as needed; existing criteria are being revised to reflect current science.

The detection limits and methods available for analyzing pollutant concentrations are not considered in setting water quality criteria. However, for other purposes, EPA has spent considerable resources in developing standard analytical methods for these pollutants in a number of matrices, and in extending detection limits to the state of the art. Analytical methods are published in 40 CFR Part 136, "Guidelines Establishing Test Procedures for the Analysis of Pollutants Under the Clean Water Act" (49 Federal Register 2, October 26, 1984). These analytical procedures are used for compliance monitoring and to express pollutant quantities, characteristics, or properties in effluent limitations guidelines and ambient water quality standards.

TABLE 1. LIST OF 126 PRIORITY POLLUTANTS

Acenaphthene	Dieldrin
Acrolein	Chlordane (tech. mixture & metabolites)
Acrylonitrile	4,4-DDT
Benzene	4,4-DDE (p,pDDX)
Benzidine	4,4-DDE (p,p-TDE)
Carbon tetrachloride (tetra-chloromethane)	Alpha-endosulfan
Chlorobenzene	Beta-endosulfan
* 1,2,4-Trichlorobenzene	Endosulfan sulfate
Hexachlorobenzene	Endrin
1,2-Dichloroethane	Endrin aldehyde
1,1-1-Trichloroethane	Methyl chloride (chloro-methane)
Hexachloroethane	Methyl bromide
* 1,1-Dichloroethane	Bromoform (tribromomethane)
1,1,2-Trichloroethane	Dichlorobromomethane
1,1,2,2,-Tetrachloroethane	Chlorodibromomethane
* Chloroethane	Hexachlorobutadiene
Bis(2-chloroethyl)ether	Hexachlorocyclopentadiene
2-Chloroethyl vinyl ether (mixed)	Isophorone
* 2-Chloronaphthalene	* Naphthalene
2,4,6-Trichlorophenol	Nitrobenzene
* Parachlorometacresol	* 2-Nitrophenol
Chloroform(trichloromethane)	* 4-Nitrophenol
2-Chlorophenol	2,4-Dinitrophenol
1,2-Dichlorobenzene	4,6-Dinitro-o-cresol
1,3-Dichlorobenzene	N-nitrosodimethylamine
1,4-Dichlorobenzene	N-nitrosodiphenylamine
3,3-Dichlorobenzidine	N-nitrosodi-n-propylamine
1,1-Dichloroethylene	Pentachlorophenol
1,2-Trans-dichloroethylene	Phenol (4APP method)
2,4-Dichlorophenol	Bis(2-ethylhexyl)phthalate
* 1,2-Dichloropropane	Butyl benzyl phthalate
1,3-Dichloropropylene	Di-n-butyl phthalate
* 2,4-Dimethylphenol	* Di-n-octyl phthalate
* 2,4-Dinitrotoluene	Diethyl phthalate
* 2,6-Dinitrotoluene	Dimethyl phthalate
1,2-Diphyenylhydrazine	Benzo(a)anthracene (1,2 benzanthracene)
Ethylbenzene	Benzo(a)pyrene(3,4-benzo-pyrene)
Fluoranthene	3,4-Benzofluoranthene
* 4-Chlorophenyl phenyl ether	Benzo(k)fluoranthane (11, 12-benzofluoranthene)
* 4-Bromophenyl phenyl ether	Chrysene
Bis(2-chloroisopropyl)ether	Acenaphthylene
* Bis(2-chloroethoxy)methane	Anthracene
Methylene chloride (dichloro-methane)	
Vinyl chloride (chloroethylene)	

TABLE 1. LIST OF 126 PRIORITY POLLUTANTS (Continued)

Aldrin
Benzo(ghi)perylene (1,12-benzoperylene)
Fluorene
Phenanthrene
Dibenzo(a,h)anthracene
Indeno(1,2,3-cd)pyrene
Pyrene
Tetrachloroethylene
Toluene
Trichloroethylene
Heptachlor
Heptachlor expoxide
Alpha-BHC
Beta-BHC
Gamma-BHC(lindane)
* Delta-BHC
PCB-1242(Aroclor 1242)
PCB-1254(Aroclor 1254)
PCB-1221(Aroclor 1221)
PCB-1232(Aroclor 1232)
PCB-1248(Aroclor 1248)
PCB-1260(Aroclor 1260)
PCB-1016(Aroclor 1016)
Toxaphene
Antimony (total)
Arsenic (total)
Asbestos (fibrous)
Beryllium (total)
Cadmium (total)
Chromium (total)
Copper (total)
Cyanide (total)
Lead (total)
Mercury (total)
Nickel (total)
Selenium (total)
Silver (total)
Thallium (total)
* Zinc (total)
2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD)

* = No Human Health Criteria

3.0 DOSE-RESPONSE ASSESSMENT

The human health risks of a substance cannot be determined with any degree of confidence unless dose-response relationships are quantified, even if the substance is known to be toxic. Therefore, a dose-response assessment is required before a criterion can be calculated. The dose-response assessment determines the quantitative relationship between the amount of exposure to a substance and the onset of toxic injury or disease. Data for determining dose-response relationships are typically derived from animal studies, or less frequently, from epidemiologic studies in exposed populations. Dose-response data for use in calculation of water quality criteria are taken from the IRIS system, described in the previous section. Data in IRIS are taken from the literature and peer reviewed within EPA before entering on the system.

The dose-response information needed for carcinogens is an estimate of the carcinogenic potency of the compound. Carcinogenic potency is defined here as a general term for a chemical's human cancer-causing potential. This term is often used loosely to refer to the more specific carcinogenic slope factor. Carcinogenic slope factor is defined here as an estimate of carcinogenic potency derived using animal studies or epidemiological data on human exposure. It is based on extrapolation from typical test exposures at high dose levels over short periods of time to more realistic low dose levels over a lifetime exposure period by using a linear model. EPA generally assumes a 70 year lifetime in these calculations. The carcinogenic slope factor is the estimate of carcinogenic potency which is used in developing the criteria. This estimate of carcinogenic potency is generally regarded as a conservative, upper bound estimate.

For non-carcinogens, EPA uses the reference dose (RfD) as the dose response parameter in calculating the criteria. The RfD was formerly referred to as an "Acceptable Daily Intake" or ADI. The RfD is useful as a reference point for gauging the potential effects of other doses. Usually, doses that are less than the RfD are not likely to be associated with any health risks, and are therefore less likely to be of regulatory concern. As the frequency of exposures exceeding the RfD increases and as

the size of the excess increases, the probability increases that adverse effects may be observed in a human population. Nonetheless, a clear conclusion cannot be categorically drawn that all doses below the RfD are "acceptable" and that all doses in excess of the RfD are "unacceptable."

In extrapolating non-carcinogen animal test data to humans, EPA uses an uncertainty factor (formerly known as a safety factor). The uncertainty factor is based upon professional judgment and ranges from 10 to 1000.

IRIS maintains files containing reference doses for chronic noncarcinogenic health effects, and slope factors and unit risks for chronic exposures to carcinogens.

4.0 EXPOSURE ASSESSMENT AND KEY ASSUMPTIONS

Once the hazard identification and dose-response assessment have been completed, the next step is exposure assessment to determine safe exposure levels. Exposure assessment is the process of characterizing the human populations exposed to the chemicals of concern, the environmental transport and fate pathways of those chemicals, and the frequency, magnitude, and duration of the exposure dose. In the water quality criteria methodology, the exposure assessment includes calculation of the ambient water concentrations which do not represent a significant risk to human health. The exposure assessments used in calculating the criteria are limited with respect to accounting for other sources of exposure to a pollutant. In the case of carcinogens, exposure assessments assume that all exposure to a pollutant occurs through ingestion of water and contaminated fish and shellfish and incremental risks are calculated on this basis. In the case of non-carcinogens, the equation used has the ability to include both intake from other dietary sources and intake from air. However, if there is insufficient data for air and other dietary sources, it is assumed that exposure is only from ingestion of water and fish.

Ideally, ambient water quality criteria should represent levels for compounds in ambient water that do not pose a hazard to human populations. However, in any realistic assessment of human health hazard, it is not possible to attain completely eliminate hazards or achieve zero risk. Ideally, criteria would be based on detailed knowledge of dose-response relationships in humans, including all sources of chemical exposure, the types of toxic effects elicited, if any, the existence of thresholds for the toxic effects, the significance of toxicant interactions, and the variances of sensitivities and exposure levels within human populations. In practice, such absolute criteria cannot be established because of deficiencies in both the available data and the means of interpreting this information. Consequently, the human health criteria proposed for carcinogens are designed to minimize, or at least specify the potential risk to humans due to substances in ambient water. Human health criteria for non-carcinogens are designed to minimize the human health hazard.

Potential social or economic costs and benefits are not considered in the formulation of the criteria. Also, analytical detection limits are not considered in recommending criteria.

In the exposure assessment, information is reviewed on current levels of human exposure to the individual pollutant from all sources. Much of the data are obtained from monitoring studies of air, water, food, soil, and human or animal tissue residues. The major purpose of this review is to provide background information on the contribution of water exposure relative to all other sources.

Information on exposure can be valuable in developing and assessing a water quality criterion. In these documents exposure from consumption of contaminated water and contaminated fish and shellfish products is used in criterion formulation. Data for all modes of exposure are useful in relating total intake to the expected contribution from contaminated water, fish, and shellfish. In addition, information on all routes of exposure, not limited to drinking water and fish and shellfish ingestion, can be used to justify or assess the feasibility of the formulation of criteria for ambient water.

In development of the criteria, several key assumptions are made and should be recognized when applying the criteria to a given situation. First, the criteria are not based on water quality monitoring data and, as noted above, the criteria represent modeled risks, as opposed to actual risks. The target population is a national average population. States may adjust the exposure assumptions to reflect local conditions, although in practice this has been the exception rather than the rule.

Second, it is important to recognize that calculation of the criteria does not take into account special groups of the population which may be more sensitive to the effects of a particular chemical, such as pregnant women, young children, or the elderly. Also, the calculation is explicitly done for a 70 kg adult. Nor does it take into account groups which may receive additional exposure to the chemical from other sources such as occupational exposure. It also does not take into account groups which may consume large quantities of fish, such as sport fishermen.

Third, exposure pathways considered in calculating the criteria are ingestion of drinking water (EPA assumes 2 liters/day contaminated at the criteria concentration), and consumption of fish (EPA assumes6.5 grams/day, contaminated at the criteria concentration multiplied by a bioconcentration factor). The assumed water consumption of 2 liters/day is taken from the National Academy of Sciences publication "Drinking Water and Health" (1977). The 2 liters/day amount was also used by EPA in calculating interim drinking water standards (NAS, 1977). This factor may be eliminated for water which is not an actual or potential source of drinking water. In the water quality criteria calculations, an estimated consumption of 6.5 grams/day is assumed for commercially and recreationally harvested fish and shellfish from estuarine and fresh waters. The value of 6.5 g/day is an average per-capita consumption rate for the U.S. population, including non-consumers (U.S. EPA, 1989). The inclusion of non-consumers may make the number somewhat under conservative. As these criteria must serve as national guidance, no attempt is made in the calculation of the criteria to account for variation among individuals in the amount of fish consumed. Also, estimates of average U.S. consumption do not account for subpopulations in areas (such as the Great Lakes) that may consume large quantities (e.g. 20 g/day) of locally caught sport fish.

The use of fish consumption as an exposure factor requires the quantification of pollutant residues in the edible portions of the ingested species. Accordingly, bioconcentration factors (BCFs) are used to relate pollutant residues in aquatic organisms to the pollutant concentration in the ambient waters in which they reside. Strictly speaking, the BCF is defined as the theoretical ratio between the concentration of a chemical in a fish and the concentration of a pollutant in the surrounding water, at equilibrium. Depending on the mechanisms and rates of chemical transfer (through the gills, through ingestion, through excretion) a fish may not be at equilibrium and therefore may exhibit a different ratio. The term bioaccumulation factor (BAF) refers to the measured value of this ratio in a field situation. The terms are frequently used imprecisely and misunderstandings can occur.

One common usage is to consider the BCF only to include intake from water, and the BAF to additionally include food input. One reason this is misleading is that BCFs so measured are often measured for short periods of time (to preclude feeding) and no equilibrium is reached. These BCFs are, therefore, frequently less than field measured BAFs. However, a true BCF represents an upper limit which should not be exceeded. Should a fish consume an amount in excess of that determined by the true BCF, it would simply excrete the excess or actually serve as a source of the pollutant to the water, through the gills. There have, however, been some studies which suggest thermodynamic equilibrium may not always be present in the environment.

Three different procedures are used to estimate the BCF, depending upon the lipid solubility of the chemical and the availability of bioconcentration data. For lipid-soluble compounds, the average BCF is calculated from the weighted average percent lipids in the edible portions of consumed freshwater and estuarine fish and shellfish. This weighted average was calculated to be 3.0 percent using data on consumption of each species and its corresponding percent lipids. Because the steady-state BCFs for lipid-soluble compounds are proportional to percent lipids in tissues, BCFs for fish and shellfish can be adjusted to the average percent lipids for aquatic organisms consumed by the U.S. population. For many lipid-soluble pollutants, at least one BCF has been determined for which the percent lipid value was measured in the exposed tissues.

With 3.0 percent as the weighted average percent lipids for freshwater and estuarine fish and shellfish in the average diet, a BCF, and a corresponding percent lipid value, the weighted average bioconcentration factor can be calculated. For example, where:

Weighted average percent lipids for average diet = 3.0 %, and
Measured BCF for Trichloroethylene with bluegills at 4.8% lipids = 17
Weighted average BCF for average diet equals:

$$BCF = 17 \times \frac{3.0\%}{4.8\%} = 10.6$$

As an estimate, 10.6 is used for the BCF for the water quality criteria.

In those cases where an appropriate bioconcentration factor is not available, the equation "Log BCF = (0.85 Log P) - 0.70" has beeen used by EPA to estimate the BCF for aquatic organisms containing about 7.6 percent lipids from the octanol/water partition coefficient P. An adjustment for percent lipids in the average diet versus 7.6 percent is made in order to derive the weighted average bioconcentration factor. There are other similar equations in general use.

For non-lipid-soluble compounds, the available BCFs for the edible portion of consumed freshwater and estuarine fish and shellfish are weighted according to consumption factors for these various types of fish to determine a weighted BCF representative of the average diet.

Human body weight is assumed to be 70 kg in calculations of ambient water quality criteria. It should be noted that this body weight is not protective of pregnant women and children. In other risk calculations, EPA has used 50 kg to represent pregnant women.

As noted in the previous sections on hazard identification and dose response relationships, the existing toxicity data must be reviewed to determine the type of effects of the chemical and the dose response relationship. If the chemical is classified as a carcinogen, it is assumed to have no threshold, and the incremental risks of developing cancer are calculated. If the compound is not classified as a carcinogen, it is assumed to have a threshold below which effects will not be observed, and the criterion is calculated based on this RfD. Examples of calculations for both a carcinogen and a noncarcinogen are given below.

4.1 Calculation of Criteria for Non-threshold Effects (Carcinogens)

After the decision has been made that a compound has the potential for causing cancers in humans, and that data exist which permit the derivation of a criterion, the water concentrations which are estimated to cause a lifetime, upper bound carcinogenic risk of 10^{-5}, 10^{-6}, and 10^{-7} are determined. The lifetime carcinogenicity

risk is the probability that a person would get cancer sometime in his or her life assuming continuous exposure to the compound.

The data used for quantitative estimates are of two types: (1) lifetime animal studies, and (2) epidemiologic studies where excess cancer risk has been associated with exposure to the agent. In animal studies it is assumed, unless evidence exists to the contrary, that if a carcinogenic response has been documented at the dose levels used in the study, then proportionately lower responses will also be observed at all lower doses, with an incidence determined by a linear extrapolation model which calculates the carcinogenic slope factor discussed in the Dose-Response Assessment Section of this report.

An example of how criteria are calculated for carcinogens is described below. Since carcinogens are assumed to have a nonthreshold dose/response characteristic, there is no recognized safe concentration for a human carcinogen. Therefore, the recommended concentration of a carcinogen in water for maximum protection of human health is zero. Because attaining a zero concentration level may not be feasible in some cases, and in order to assist EPA and the States in the possible future development of water quality regulations, concentrations of the carcinogenic compound corresponding to several incremental lifetime cancer risk levels are estimated. A cancer risk level provides an estimate of the additional incidence of cancer that may be expected in an exposed population. A risk of 10^{-5} for example, indicates a probability of one additional case of cancer for every 100,000 people exposed; a risk of 10^{-6} indicates one additional case of cancer for every million people exposed, and so forth.

For carcinogens, the criteria calculation is as follows:

$$\text{Criterion} = \frac{\text{(body weight x risk level)}}{\text{potency x (water consumption + fish consumption x BCF)}}$$

The calculations for hexachlorobutadiene (HCBD) are described here as an example of criteria formulation for a carcinogen. HCBD is produced in the United States as a by-product of the manufacture of chlorinated hydrocarbons such as

tetracholoethylene, trichloroethylene, and carbon tetrachloride. It is used as a solvent for many organic substances. HCBD has a low vapor pressure and, thus, may not volatilize rapidly from the aqueous environment to the atmosphere. Concentrations observed in water indicate the HCBD may be quite persistent in the environment. It may also be adsorbed onto the sediments, particularly in areas high in organic content.

Review of toxicity literature indicates the kidney appears to be the organ most sensitive to HCBD. The carcinogenic effects of renal tubular adenomas and adenocarcinomas were strongly demonstrated at a dosage of 20 mg/kg/day in the diet in rats in a two year feeding study. Incidence rates for dose levels of 0.0, 0.2, 2.0, and 20.0 were 1/90, 0/40, 0/40, and 9/39, respectively. A q_1^* (carcinogenic slope factor) value of 0.07752 $(mg/kg/day)^{-1}$ was calculated from the rat study data.

Bioconcentration factors are available for HCBD but the necessary data concerning percent lipids are not. Therefore, the equation "Log BCF = (0.85 Log P) - 0.70" can be used to estimate the BCF for aquatic organisms that contain about 7.6 percent lipids from the octanol/water partition coefficient (P). Based on a measured log P value of 1.82, the steady-state bioconcentration factor for HCBD is estimated to be 7.03. An adjustment factor of 3.0/7.6 = 0.395 can be used to adjust the estimated BCF from 7.6 percent lipids (on which the equation is based), to the 3.0 percent lipids, which is the weighted average for consumed fish and shellfish. Thus, the weighted average bioconcentration factor for HCBD and the edible portion of all freshwater and estuarine aquatic organisms consumed by the U.S. population is calculated to be 7.03 x 0.395 = 2.78.

Parameters used in calculation of the criterion for the 10^{-6} risk level are as follows:

Body weight = 70 kg
Risk level = 10^{-6}
Potency = 0.07752 $(mg/kg/day)^{-1}$
Water consumption = 2 liters/day
Fish consumption = 6.5 grams/day = 0.0065 kg/day
Bioconcentration factor = 2.78

The calculation of an ambient water quality criterion for HCBD based on fish consumption at the 10^{-6} risk level using the formula given above is as follows:

$$\text{Criterion} = \frac{(70 \text{ kg} \times 10^{-6})}{0.07752 \text{ (mg/kg/day)}^{-1} \times (2 \text{ liters/day} + 0.0065 \text{ kg/day} \times 2.78)}$$

$$= 0.45 \text{ ug/L}$$

The criteria for the upper bound risk levels of 10^{-5} and 10^{-7} are 4.5 ug/L and 0.045 ug/L, respectively, assuming consumption of 2 liters of drinking water and 6.5 grams of fish and shellfish per day. Approximately one percent of the HCBD exposure results from consumption of aquatic organisms. If the exposure is assumed to be from fish alone, the water quality criteria associated with risk levels of 10^{-5}, 10^{-6}, and 10^{-7} are 500 ug/L, 50 ug/L, and 5.00 ug/L, respectively.

4.2 Calculation of Criteria for Threshold Effects

In developing guidelines for deriving criteria based on noncarcinogenic responses, five types of response levels are considered:

NOEL: No-Observed-Effect Level

NOAEL: No-Observed-Adverse-Effect Level

LOEL: Lowest-Observed-Effect Level

LOAEL: Lowest-Observed-Adverse-Effect Level

FEL: Frank-Effect Level

Adverse effects are defined as any effects which result in functional impairment and/or pathological lesions which may affect the performance of the whole organism, or which reduce an organism's ability to respond to an additional challenge. Available data on the five types of effects are evaluated to determine the threshold effects

concentration, and to estimate an RfD. In determining an RfD, an uncertainty factor (formerly referred to as a safety factor) ranging from 10 to 1000 is applied to the estimated threshold level, depending on the confidence in the available data. When the quality and quantity of experimental data are satisfactory, a low uncertainty factor is used; when data are judged to be inadequate or equivocal, a larger uncertainty factor is used. In other words, uncertainty factors are assigned on a case specific basis based on somewhat subjective judgements of the quality and quantity of the data. EPA maintains a data base on reference doses (RfDs) in the IRIS system. The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious effects during a lifetime. RfDs are based on an assumption of long-term exposure and may not be appropriately applied to short-term exposure situations.

For threshold chemicals (noncarcinogens), the criteria are based on an RfD, and dietary and inhalation exposures are considered where data is available. The formula is:

$$\text{Criterion} = \frac{\text{RfD - (dietary intake + air intake)}}{\text{(water consumption + fish consumption x BCF)}}$$

Toluene is used below as an example for calculation of criteria for a threshold chemical. Toluene is used in the production of benzene and other chemicals as well as being used directly in gasoline and as a solvent. Although it is volatile, it has been detected in finished water supplies at levels ranging from 0.1 ug/L to 11 ug/L.

A number of investigations of the subacute and chronic toxicity of toluene have been conducted. Although most were inhalation studies, at least one long-term oral dosing study was conducted in which female rats were given toluene at 118, 354, and 590 mg/kg in olive oil by stomach tube five times weekly for 193 days. No adverse effects on growth appearance and behavior, mortality, organ/body weights, blood urea nitrogen levels, bone marrow counts, peripheral blood counts, or morphology of major

organs were observed at any dose level. The lack of toxicity reported in this study is supported by findings of other groups of investigators who found no evidence of residual injury in a variety of animal species subjected to toluene vapor for varying times over periods as long as 18 months. Therefore, the highest dose utilized in the oral study, 590 mg/kg was used as the basis for calculating the RfD for toluene. Since no other data were available on effects at higher levels, 590 mg/kg was assumed to be the "maximum-no-effect" dose. However, since the highest dose had no observed effect, no information was available on the lowest observed effects. A single oral dose of 2.4 g/kg had no hepatotoxic effects in rats and the oral LD_{50} for toluene in young adult rats was found to be 7.0 g/kg. It is possible that the actual "maximum-no-effect" dose may be lower than 590 mg/kg, should alternative indices of toxicity be evaluated. Humans may prove to be more sensitive to toluene than experimental animals. Thus, a safety factor of 1,000 was applied. Assuming a body weight of 70 kg and adjusting for the dosing of five times per week, the RfD is calculated as follows:

$$\text{RfD} = \frac{590 \text{ mg/kg} \times 70 \text{ kg} \times 5/7 \text{ day}}{1{,}000} = 29.5 \text{ mg/day}$$

It is assumed that 100 percent of man's exposure comes from water. Although it is desireable to arrive at a criterion level for water based upon total exposure potential, the database for exposures other than water is not sufficient to allow a factoring of air intake and dietary intake (other than fish and shellfish) into the calculation of the criterion.

No measured steady-state bioconcentration factor (BCF) was available for toluene. Therefore, the equation "Log BCF = (0.85 Log P) - 0.70" was used to estimate the BCF for aquatic organisms that contain about 7.6% lipids for the octanol water partition coefficient (P). Based on an average measured Log P value of 2.51, the steady-state bioconcentration factor for toluene is estimated to be 27.1. An adjustment factor of 3.0/7.6 = 0.395 can be used to adjust the estimated BCF from

7.6% lipids (on which the equation is based) to 3.0% lipids, is the weighted average for consumed fish and shellfish. Thus, the weighted average bioconcentration factor for toluene and the edible portion of all freshwater and estuarine aquatic organisms consumed by the U.S. population is calculated to be 27.1 x 0.395 = 10.7

Consumption of 2 liters of water daily and 6.5 g of contaminated fish having a bioconcentration factor of 10.7, would result in, assuming 100% gastrointestinal absorption of toluene, a maximum permissible concentration of 14.3 mg/L for the ingested water:

$$\text{Criterion} = \frac{29.5 \text{ mg/day}}{2 \text{ L} + (10.7 \times 0.0065)} = 14.3 \text{ mg/L}$$

Drinking water contributes 97% of the assumed exposure, while eating contaminated fish products accounts for 3%. The criterion level for toluene can alternatively be expressed as 424 mg/L if exposure is assumed to be from the consumption of fish and shellfish products alone.

The principal goal of the water quality criteria program is to provide guidance for maintaining acceptable water quality under a program for source reduction. The development of an acceptable level for fish tissue is not a goal of the water quality criteria methodology, and the SAB did not review the methodology for this use. However, by taking the criteria and multiplying by the BCF factor used in its derivation, an implicit fish tissue level may be calculated. This could then be used to establish a fish contamination advisory, if measured fish levels exceed this level. This calculation is the same for carcinogens and non-carcinogens. For example, using the criterion for toluene, the acceptable fish tissue level would be calculated as follows:

Acceptable fish tissue level = Criterion x BCF = 14.3 ppm x 10.7 = 153 ppm

5.0 RISK MANAGEMENT DECISION

Water quality criteria for the protection of human health are issued as guidance for making risk management decisions. These criteria present scientific data and guidance on the environmental effects of pollutants which can be used to derive regulatory requirements for water quality, such as State water quality standards. The criteria are EPA's recommended ambient water concentrations which EPA believes do not represent a significant risk to human health. States are free to make risk level determinations as part of their risk management process.

The water quality criteria methodology is purely a risk assessment as opposed to a risk management process. No benefits analysis is considered, nor are costs. The differences between carcinogens and non-carcinogens involve the dose-response factors described above. For non-carcinogens, the risk assessment leads to a one value criterion. For carcinogens, the assessment leads to a series of criteria associated with incremental increases in the risk of developing cancer. The criteria are calculated for individual chemicals with no consideration of additive, synergistic, or antagonistic effects in mixtures.

Also, the criteria do not take into account special populations which may be at additional risk, such as sport fisherman or regional populations who consume quantities of fish much higher than the national average. If the conditions within a State differ from the assumptions made in calculation of the criteria, the States have the options to perform their own risk assessments and to set standards which more accurately reflect their specific conditions and which provide adequate protection for human health.

6.0 REFERENCES

40 Code of Federal Regulations (CFR), Part 136, "Guidelines Establishing Test Procedures for the Analysis of Pollutants Under the Clean Water Act". (49 Federal Register 2, October 26, 1984).

45 Federal Register 79347, "Water Quality Criteria Documents; Availability, Appendix C - Guidelines and Methodology Used in the Preparation of Health Effect Assessment Chapters of the Consent Decree Water Criteria Documents" November 28, 1980.

National Academy of Sciences (NAS), 1977. "Drinking Water and Health".

U.S. Environmental Protection Agency (U.S. EPA), 1989. "Assessing Human Health Risks from Chemically Contaminated Fish and Shellfish: A Guidance Manual". EPA-503/8-89-002. September.

APPENDIX A

WATER QUALITY CRITERIA DOCUMENTS; AVAILABILITY

(45 Federal Register 79318)

federal register

Friday
November 28, 1980

Part V

Environmental Protection Agency

Water Quality Criteria Documents; Availability

ENVIRONMENTAL PROTECTION AGENCY

[FRL 1623-3]

Water Quality Criteria Documents; Availability

AGENCY: Environmental Protection Agency.

ACTION: Notice of Water Quality Criteria Documents.

SUMMARY: EPA announces the availability and provides summaries of water quality criteria documents for 64 toxic pollutants or pollutant categories. These criteria are published pursuant to section 304(a)(1) of the Clean Water Act.

AVAILABILITY OF DOCUMENTS: Summaries of both aquatic-based and health-based criteria from the documents are published below. Copies of the complete documents for individual pollutants may be obtained from the National Technical Information Service (NTIS), 5285 Port Royal Road, Springfield, VA 22161, (703-487-4650). A list of the NTIS publication order numbers for all 64 criteria documents is published below. These documents are also available for public inspection and copying during normal business hours at: Public Information Reference Unit, U.S. Environmental Protection Agency, Room 2404 (rear), 401 M St., S.W., Washington, D.C. 20460. As provided in 40 CFR Part 2, a reasonable fee may be charged for copying services. Copies of these documents are also available for review in the EPA Regional Office libraries.

Copies of the documents are not available from the EPA office listed below. Requests sent to that office will be forwarded to NTIS or returned to the sender.

1. Acenaphthene, PB81-117269.
2. Acrolein, PB81-117277.
3. Acrylonitrile, PB81-117285.
4. Aldrin/Dieldrin, PB81-117301.
5. Antimony, PB81-117319.
6. Arsenic, PB81-117327.
7. Asbestos, PB81-117335.
8. Benzene, PB81-117293.
9. Benzidine, PB81-117343.
10. Beryllium, PB81-117350.
11. Cadmium, PB81-117368.
12. Carbon Tetrachloride, PB81-117376.
13. Chlordane, PB81-117384.
14. Chlorinated benzenes, PB81-117392.
15. Chlorinated ethanes, PB81-117400.
16. Chloroalkyl ethers, PB81-117418.
17. Chlorinated naphthalene, PB81-117426.
18. Chlorinated phenols, PB81-117434.
19. Chloroform, PB81-117442.
20. 2-chlorophenol, PB81-117459.
21. Chromium, PB81-117467.
22. Copper, PB81-117475.
23. Cyanides, PB81-117483.
24. DDT, PB81-117491.
25. Dichlorobenzenes, PB81-117509.
26. Dichlorobenzidine, PB81-117517.
27. Dichloroethylenes, PB81-117525.
28. 2,4-dichlorophenol, PB81-117533.
29. Dichloropropanes/propenes, PB81-117541.
30. 2,4-dimethylphenol, PB81-117558.
31. Dinitrotoluene, PB81-117566.
32. Diphenylhydrazine, PB81-117731.
33. Endosulfan, PB81-117574.
34. Endrin, PB81-117582.
35. Ethylbenzene, PB81-117590.
36. Fluoranthene, PB81-117608.
37. Haloethers, PB81-117616.
38. Halomethanes, PB81-117624.
39. Heptachlor, PB81-117632.
40. Hexachlorobutadiene, PB81-117640.
41. Hexachlorocyclohexane, PB81-117657.
42. Hexachlorocyclopentadiene, PB81-117665.
43. Isophorone, PB81-117673.
44. Lead, PB81-117681.
45. Mercury, PB81-117699.
46. Naphthalene, PB81-117707.
47. Nickel, PB81-117715.
48. Nitrobenzene, PB81-117723.
49. Nitrophenols, PB81-117749.
50. Nitrosamines, PB81-117756.
51. Pentachlorophenol, PB81-117764.
52. Phenol, PB81-117772.
53. Phthalate esters, PB81-117780.
54. Polychlorinated biphenyls (PCBs), PB81-117798.
55. Polynuclear aromatic hydrocarbons, PB81-117806.
56. Selenium, PB81-117814.
57. Silver, PB81-117822.
58. Tetrachloroethylene, PB81-117830.
59. Thallium, PB81-117848.
60. Toluene, PB81-117855.
61. Toxaphene, PB81-117863.
62. Trichloroethylene, PB81-117871.
63. Vinyl chloride, PB81-117889.
64. Zinc, PB81-117897.

FOR FURTHER INFORMATION CONTACT: Dr. Frank Gostomski, Criteria and Standards Division (WH-585), United States Environmental Protection Agency, 401 M Street, S.W., Washington, D.C. 20460, (202) 245-3042.

SUPPLEMENTARY INFORMATION:

Background

Pursuant to section 304(a)(1) of the Clean Water Act, 33 U.S.C. 1314(a)(1), EPA is required to periodically review and publish criteria for water quality accurately reflecting the latest scientific knowledge:

(A) on the kind and extent of all identifiable effects on health and welfare including, but not limited to, plankton, fish, shellfish, wildlife, plant life, shorelines, beaches, esthetics, and recreation which may be expected from the presence of pollutants in any body of water, including groundwater, (B) on the concentration and dispersal of pollutants, or their byproducts, through biological, physical, and chemical processes, and (C) on the effects of pollutants on biological community diversity, productivity, and stability, including information on the factors affecting rates of eutrophication and rates of organic and inorganic sedimentation for varying types of receiving waters.

EPA is today announcing the availability of criteria documents for 64 of the 65 pollutants designated as toxic under section 307(a)(1) of the Act. The document on TCDD (Dioxin) will be published within the next month after review of recent studies. Criteria for the section 307(a)(1) toxic pollutants being published today will replace the criteria for those same pollutants found in the EPA publication, *Quality Criteria for Water*, (the "Red Book.") Criteria for all other pollutants and water constituents found in the "Red Book" remain valid. The criteria published today have been derived using revised methodologies for determining pollutant concentrations that will, when not exceeded, reasonably protect human health and aquatic life. Draft criteria documents were made available for public comment (44 FR 15926, March 15, 1979, 44 FR 43660, July 25, 1979, 44 FR 56628, October 1, 1979). These final criteria have been derived after consideration of all comments received.

These criteria documents are also issued in satisfaction of the Settlement Agreement in *Natural Resources Defense Council, et al.* v. *Train*; 8 E.R.C. 2120 (1976), modified, 12 E.R.C. 1833 (D.D.C. 1979). Pursuant to paragraph 11 of that agreement, EPA is required to publish criteria documents for the 65 pollutants which Congress, in the 1977 amendments to the Act, designated as toxic under section 307(a)(1). These documents contain recommended maximum permissible pollutant concentrations consistent with the protection of aquatic organisms, human health, and some recreational activities. Although paragraph 11 imposes certain obligations on the Agency, it does not create additional authority.

The Development of Water Quality Criteria

Section 304(a)(1) criteria contain two essential types of information: (1) discussions of available scientific data on the effects of pollutants on public health and welfare, aquatic life and recreation, and (2) quantitative concentrations or qualitative assessments of the pollutants in water which will generally ensure water

quality adequate to support a specified water use. Under section 304(a)(1), these criteria are based solely on data and scientific judgments on the relationship between pollutant concentrations and environmental and human health effects. Criteria values do not reflect considerations of economic or technological feasibility.

Publication of water quality criteria of this type has been an ongoing process which EPA, and its predecessor Agency, the Federal Water Pollution Control Administration, have been engaged in since 1968. At that time the first Federal compilation of water quality criteria, the so-called "Green Book" *(Water Quality Criteria)*, was published. As now, these criteria contained both narrative discussions of the environmental effects of pollutants on a range of possible uses and concentrations of pollutants necessary to support these uses. Since that time, water quality criteria have been revised and expanded with publication of the "Blue Book" *(Water Quality Criteria 1972)* in 1973 and the "Red Book" *(Quality Criteria for Water)* in 1976.

Since publication of the Red Book there have been substantial changes in EPA's approach to assessing scientific data and deriving section 304(a)(1) criteria. Previous criteria were derived from a limited data base. For many pollutants, an aquatic life criterion was derived by multiplying the lowest concentration known to have acute lethal effect on half of a test group of an aquatic species (the LC50 value) by an application factor in order to protect against chronic effects. If data showed a substance to be bioaccumulative or to have other significant long-term effects, a factor was used to reduce the indicated concentrations to a level presumed to be protective. Criteria for the protection of human health were similarly derived by considering the pollutants' acute, chronic, and bioaccumulative effects on non-human mammals and humans.

Although a continuation of the process of criteria development, the criteria published today were derived using revised methodologies (Guidelines) for calculating the impact of pollutants on human health and aquatic organisms. These Guidelines consist of systematic methods for assessing valid and appropriate data concerning acute and chronic adverse effects of pollutants on aquatic organisms, non-human mammals, and humans. By use of these data in prescribed ways, criteria are formulated to protect aquatic life and human health from exposure to the pollutants. For some pollutants, bioconcentration properties are used to formulate criteria protective of aquatic life uses. For almost all of the pollutants, bioconcentration properties are used to assess the relative extent of human exposure to the pollutant either directly through ingestion of water or indirectly through consumption of aquatic organisms. Human health criteria for carcinogens are presented as incremental risks to man associated with specific concentrations of the pollutant in ambient water. The Guidelines used to derive criteria protective of aquatic life and human health are fully described in appendices B and C, respectively, of this Notice.

The Agency believes that these Guidelines provide criteria which more accurately reflect the effects of these pollutants on human health and on aquatic organisms and their uses. They are based on a more rational and consistent approach for using scientific data. These Guidelines were developed by EPA scientists in consultation with scientists from outside the Agency and they have been subjected to intensive public comment.

Neither the Guidelines nor the criteria are considered inflexible doctrine. Even at this time, EPA is taking action to employ the resources of peer review groups, including the Science Advisory Board, to evaluate recently published data, and EPA is conducting its own evaluation of new data to determine whether revisions to the criteria documents would be warranted.

The criteria published today are based solely on the effect of a single pollutant. However, pollutants in combination may have different effects because of synergistic, additive, or antagonistic properties. It is impossible in these documents to quantify the combined effects of these pollutants, and persons using criteria should be aware that site-specific analysis of actual combinations of pollutants may be necessary to give more precise indications of the actual environmental impacts of a discharge.

Relationship of the Section 304(a)(1) Criteria to Regulatory Programs

Section 304(a)(1) criteria are not rules and they have no regulatory inpact. Rather, these criteria present scientific data and guidance on the enviromental effect of pollutants which can be useful to derive regulatory requirements based on considerations of water quality impacts. Under the Clean Water Act, these regulatory requirements may include the promulgation of water quality-based effluent limitations under section 302, water quality standards under section 303, or toxic pollutant effluent standards under section 307. States are encouraged to begin to modify or, if necessary, develop new programs necessary to support the implementation of regulatory controls for toxic pollutants. As appropriate, States may incorporate criteria for toxic pollutants, based on this guidance, into their water quality standards.

Section 304(a)(1) criteria have been most closely associated with the development of State water quality standards, and the "Red Book" values have, in the past, been the basis for EPA's assessments of the adequacy of State requirements. However, EPA is now completing a major review of its water quality standards policies and regulations. After consideration of comments received on an Advance Notice of Proposed Rulemaking (43 FR 29588, July 10, 1978) and the draft criteria documents, the Agency intends to propose, by the end of this year, a revised water quality standards regulation which will clarify the Agency's position on a number of significant standards issues.

With the publication of these criteria, however, it is appropriate to discuss EPA's current thinking on standards issues relating to their use. This discussion does not establish new regulatory requirements and is intended as guidance on the possible uses of these criteria and an indication of future rulemaking the Agency may undertake. No substantive requirements will be established without further opportunity for public comment.

Water Quality Standards

Section 303 of the Clean Water Act provides that water quality standards be developed for all surface waters. A water quality standard consists basically of two parts: (1) A "designated use" for which the water body is to be protected (such as "agricultural," "recreation" or "fish and wildlife"), and (2) "criteria" which are numerical pollutant concentration limits or narrative statements necessary to preserve or achieve the designated use. A water quality standard is developed through State or Federal rulemaking proceedings and must be translated into enforceable effluent limitations in a point source (NPDES) permit or may form the basis of best management practices applicable to nonpoint sources under section 208 of the Act.

Relationship of Section 304(a)(1) Criteria to the Criteria Component of State Water Quality Standards:

In the ANPRM, EPA announced a policy of "presumptive applicability" for

section 304(a)(1) criteria codified in the "Red Book." Presumptive applicability meant that a State had to adopt a criterion for a particular water quality parameter at least as stringent as the recommendation in the Red Book unless the State was able to justify a less stringent criterion based on: natural background conditions, more recent scientific evidence, or local, site-specific information. EPA is rescinding the policy of presumptive applicability because it has proven to be too inflexible in actual practice.

Although the section 304(a)(1) criteria represent a reasonable estimate of pollutant concentrations consistent with the maintenance of designated water uses, States may appropriately modify these values to reflect local conditions. In certain circumstances, the criteria may not accurately reflect the toxicity of a pollutant because of the effect of local water quality characteristics or varying sensitivities of local populations. For example, in some cases, ecosystem adaptation may enable a viable, balanced aquatic population to exist in waters with high natural background levels of certain pollutants. Similarly, certain compounds may be more or less toxic in some waters because of differences in alkalinity, temperature, hardness, and other factors.

Methods for adjusting the section 304(a)(1) criteria to reflect these local differences are discussed below.

Relationship of Section 304(a)(1) Criteria to Designated Water Uses:

The criteria published today can be used to support the designated uses which are generally found in State standards. The following section discusses the relationship between the criteria and individual use classifications. Where a water body is designated for more than one use, criteria necessary to protect the most sensitive use should be applied.

1. *Recreation:* Recreational uses of water include such activities as swimming, wading, boating and fishing. Although insufficient data exist on the effects of toxic pollutants resulting from exposure through such primary contact as swimming, section 304(a)(1) criteria based on human health effects may be used to support this designated use where fishing is included in the State definition of "recreation." In this situation only the portion of the criterion based on fish consumption should be used.

2. *Protection and Propagation of Fish and Other Aquatic Life:* The section 304(a)(1) criteria based on toxicity to aquatic life may be used directly to support this designated use.

3. *Agricultural and Industrial Uses:* The section 304(a)(1) criteria were not specifically developed to reflect the impact of pollutants on agricultural and industrial uses. However, the criteria developed for human health and aquatic life are sufficiently stringent to protect these other uses. States may establish criteria specifically designed to protect these uses.

4. *Public Water Supply:* The drinking water exposure component of the human health effects criteria can apply directly to this use classification or may be appropriately modified depending upon whether the specific water supply system falls within the auspices of the Safe Drinking Water Act's (SDWA) regulatory control, and the type and level of treatment imposed upon the supply before delivery to the consumer. The SDWA controls the presence of toxic pollutants in finished ("end-of-tap") drinking water. A brief description of relevant sections of this Act is necessary to explain how the SDWA will work in conjunction with section 304(a)(1) criteria in protecting human health from the effects of toxics due to consumption of water.

Pursuant to section 1412 of the SDWA, EPA has promulgated "National Interim Primary Drinking Water Standards" for certain organic and inorganic substances. These standards establish "maximum contaminant levels" ("MCLs") which specify the maximum permissible level of a contaminant in water which may be delivered to a user of a public water system now defined as serving a minimum of 25 people. MCLs are established based on consideration of a range of factors including not only the health effects of the contaminants but also technological and economic feasibility of the contaminants' removal from the supply. EPA is required to establish revised primary drinking water regulations based on the effects of a contaminant on human health, and include treatment capability, monitoring availability, and costs. Under Section 1401(1)(D)(i) of the SDWA, EPA is also allowed to establish the minimum quality criteria for water which may be taken into a public water supply system.

Section 304(a)(1) criteria provide estimates of pollutant concentrations protective of human health, but do not consider treatment technology, costs and other feasibility factors. The section 304(a)(1) criteria also include fish bioaccumulation and consumption factors in addition to direct human drinking water intake. These numbers were not developed to serve as "end of tap" drinking water standards, and they have no regulatory significance under the SDWA. Drinking water standards are established based on considerations, including technological and economic feasibility, not relevant to section 304(a)(1) criteria. Section 304(a)(1) criteria may be analogous to the recommended maximum contaminant levels (RMCLs) under section 1412(b)(1)(B) of the SDWA in which, based upon a report from the National Academy of Sciences, the Administrator should set target levels for contaminants in drinking water at which "no known or anticipated adverse effects occur and which allows an adequate margin of safety". RMCLs do not take treatment, cost, and other feasibility factors into consideration. Section 304(a)(1) criteria are, in concept, related to the health-based goals specified in the RMCLs. Specific mandates of the SDWA such as the consideration of multi-media exposure, as well as different methods for setting maximum contaminant levels under the two Acts, may result in differences between the two numbers.

MCLs of the SDWA, where they exist, control toxic chemicals in finished drinking water. However, because of variations in treatment and the fact that only a relatively small number of MCLs have been developed, ambient water criteria may be used by the States as a supplement to SDWA regulations. States will have the option of applying MCLs, section 304(a)(1) human health effects criteria, modified section 304(a)(1) criteria or controls more stringent than these three to protect against the effects of toxic pollutants by ingestion from drinking water.

For untreated drinking water supplies, States may control toxics in the ambient water through either use of MCLs (if they exist for the pollutants of concern), section 304(a)(1) human health effects criteria, or a more strigent contaminant level than the former two options.

For treated drinking water supplies serving less than 25 people, States may choose toxics control through application of MCLs (if they exist for the pollutants of concern and are attainable by the type of treatment) in the finished drinking water. States also have the options to control toxics in the ambient water by choosing section 304(a)(1) criteria, adjusted section 304(a)(1) criteria resulting from the reduction of the direct drinking water exposure component in the criteria calculation to the extent that the treatment procedure reduces the level of pollutants, or a more stringent contaminant level than the former three options.

For treated drinking water supplies serving 25 people or greater, States *must* control toxics down to levels at least as stringent as MCLs (where they exist for

the pollutants of concern) in the finished drinking water. However, States also have the options to control toxics in the ambient water by choosing section 304(a)(1) criteria, adjusted section 304(a)(1) criteria resulting from the reduction of the direct drinking water exposure component in the criteria calculation to the extent that the treatment process reduces the level of pollutants, or a more stringent contaminant level than the former three options.

Inclusion of Specific Pollutants in State Standards:

To date, EPA has not required that a State address any specific pollutant in its standards. Although all States have established standards for most conventional pollutants, the treatment of toxic pollutants has been much less extensive. In the ANPRM, EPA suggested a policy under which States would be required to address a set of pollutants and incorporate specific toxic pollutant criteria into water quality standards. If the State failed to incorporate these criteria, EPA would promulgate the standards based upon these criteria pursuant to section 303(c)(4)(B).

In the forthcoming proposed revision to the water quality standard regulations, a significant change in policy will be proposed relating to the incorporation of certain pollutants in State water quality standards. This proposal will differ from the proposal made in the ANPRM. The ANPRM proposed an EPA-published list of pollutants for which States would have had to develop water quality standards. This list might have contained some (or all) of the 65 toxic pollutants. However, the revised water quality standards regulation will propose a process by which EPA will assist States in identifying specific toxic pollutants required for assessment for possible inclusion in State water quality standards. For these pollutants, States will have the option of adopting the published criteria or of adjusting those criteria based on site-specific analysis.

These pollutants would generally represent the greatest threat to sustaining a healthy, balanced ecosystem in water bodies or to human health due to exposure directly or indirectly from water. EPA is currently developing a process to determine which pollutants a State must assess for possible inclusion in its water quality standards. Relevant factors might include the toxicity of the pollutant, the frequency and concentration of its discharge, its geographical distribution, the breadth of data underlying the scientific assessment of its aquatic life and human health effects, and the technological and economic capacity to control the discharge of the pollutant. For some of the pollutants, all States may be required to assess them for possible inclusion in their standards. For others, assessment would be restricted to States or limited to specific water bodies where the pollutants pose a particular site-specific problem.

Criteria Modification Process

Flexibility is available in the application of these and any other valid water quality criteria to regulatory programs. Although in some cases they may be used by the States as developed, the criteria may be modified to refect local environmental conditions and human exposure patterns before incorporation into programs such as water quality standards. If significant impacts of site-specific water quality conditions in the toxicities of pollutants can be demonstrated or significantly different exposure patterns of these pollutants to humans can be shown, section 304(a)(1) criteria may be modified to reflect these local conditions. The term "local" may refer to any appropriate geographic area where common aquatic environmental conditions or exposure patterns exist. Thus, "local" may signify a Statewide, regional, river reach, or entire river basin area. On the other hand, the criteria of some pollutants might be applicable nationwide without the need for adaptation to reflect local conditions. The degree of toxicity toward aquatic organisms and humans characteristic of these pollutants would not change significantly due to local water quality conditions.

EPA is examining a series of environmental factors or water quality parameters which might realistically be expected to affect the laboratory-derived water quality criterion recommendation for a specific pollutant. Factors such as hardness, pH, suspended solids, types of aquatic organisms present, etc. could impact on the chemical's effect in the aquatic environment. Therefore, local information can be assembled and analyzed to adjust the criterion recommendation if necessary.

The Guidelines for deriving criteria for the protection of aquatic life suggest several approaches for modifying the criteria. First, toxicity data, both acute and chronic, for local species could be substituted for some or all of the species used in deriving criteria for the water quality standard. The minimum data requirements should still be fulfilled in calculating a revised criterion. Second, criteria may be specifically tailored to a local water body by use of data from toxicity tests performed with that ambient water. A procedure such as this would account for local environmental conditions in formulating a criterion relevant to the local water body. Third, site-specific water quality characteristics resulting in either enhancement or mitigation of aquatic life toxicity for the pollutant could be factored into final formulation of the criterion. Finally, the criteria may be made more stringent to ensure protection of an individual species not otherwise adequately protected by any of the three modification procedures previously mentioned.

EPA does not intend to have States assess every local stream segment and lake in the country on an individual basis before determining if an adjustment is necessary. Rather, it is envisioned that water bodies having similar hydrological, chemical, physical, and biological properties will be grouped for the purpose of criteria adjustment. The purpose of this effort is to assist States in adapting the section 304(a) criteria to local conditions where needed, thereby precluding the setting of arbitrary and perhaps unnecessarily stringent or underprotective criteria in a water body. In all cases, EPA will still be required, pursuant to section 303(c), to determine whether the State water quality standards are consistent with the goals of the Act, including a determination of whether State-established criteria are adequate to support a designated use.

Criteria for the Protection of Aquatic Life

Interpretation of the Criteria

The aquatic life criteria issued today are summarized in Appendix A of this Federal Register notice. Criteria have been formulated by applying a set of Guidelines to a data base for each pollutant. The criteria for the protection of aquatic life specify pollutant concentrations which, if not exceeded, should protect most, but not necessarily all, aquatic life and its uses. The Guidelines specify that criteria should be based on an array of data from organisms, both plant and animal, occupying various trophic levels. Based on these data, criteria can be derived which should be adequate to protect the types of organisms necessary to support an aquatic community.

The Guidelines are not designed to derive criteria which will protect all life stages of all species under all conditions. Generally some life stage of one or more tested species, and

probably some untested species, will have sensitivities below the maximum value or the 24-hour average under some conditions and would be adversely affected if the highest allowable pollutant concentrations and the worst conditions existed for a long time. In actual practice, such a situation is not likely to occur and thus the aquatic community as a whole will normally be protected if the criteria are not exceeded. In any aquatic community there is a wide range of individual species sensitivities to the effects of toxic pollutants. A criterion adequate to protect the most susceptible life stage of the most sensitive species would in many cases be more stringent than necessary to protect the overall aquatic community.

The aquatic life criteria specify both maximum and 24-hour average values. The combination of the two values is designed to provide adequate protection of aquatic life and its uses from acute and chronic toxicity and bioconcentration without being as restrictive as a one-number criterion would have to be to provide the same amount of protection. A time period of 24 hours was chosen in order to ensure that concentrations not reach harmful levels for unacceptably long periods. Averaging for longer periods, such as a week or a month for example, could permit high concentrations to persist long enough to produce significant adverse effects. A 24-hour period was chosen instead of a slightly longer or shorter period in recognition of daily fluctuations in waste discharges and of the influence of daily cycles of sunlight and darkness and temperature on both pollutants and aquatic organisms.

The maximum value, which is derived from acute toxicity data, prevents significant risk of adverse impact to organisms exposed to concentrations above the 24-hour average. Merely specifying the average value over a specified time period is insufficient because concentrations of chemicals higher than the average value can kill or cause irreparable damage in short periods. Furthermore, for some chemicals the effect of intermittent high exposures is cumulative. It is therefore necessary to place an upper limit on pollutant concentrations to which aquatic organisms might be exposed. The two-number criterion is intended to describe the highest average ambient water concentration which will produce a water quality generally suited to the maintenance of aquatic life while restricting the extent and duration of the excursions over that average to levels which will not cause harm. The only way to assure the same degree of protection with a one-number criterion would be to use the 24-hour average as a concentration that is not to be exceeded at any time in any place.

Since some substances may be more toxic in freshwater than in saltwater, or vice versa, provision is made for deriving separate water quality criteria for freshwater and for saltwater for each substance. However, for some substances sufficient data may not be available to derive one or both of these criteria using the Guidelines.

Specific aquatic life criteria have not been developed for all of the 65 toxic pollutants. In those cases where there were insufficient data to allow the derivation of a criterion, narrative descriptions of apparent threshold levels for acute and/or chronic effects based on the available data are presented. These descriptions are intended to convey a sense of the degree of toxicity of the pollutant in the absence of a criterion recommendation.

Summary of the Aquatic Life Guidelines

The Guidelines for Deriving Water Quality Criteria for the Protection of Aquatic Life and its Uses were developed to describe an objective, internally consistent, and appropriate way of ensuring that water quality criteria for aquatic life would provide, on the average, a reasonable amount of protection without an unreasonable amount of overprotection or underprotection. The resulting criteria are not intended to provide 100 percent protection of all species and all uses of aquatic life all of the time, but they are intended to protect most species in a balanced, healthy aquatic community. The Guidelines are published as Appendix B of this Notice. Responses to public comments on these Guidelines are attached as Appendix D.

Minimum data requirements are identified in four areas: acute toxicity to animals (eight data points), chronic toxicity to animals (three data points), toxicity to plants, and residues. Guidance is also given for discarding poor quality data.

Data on acute toxicity are needed for a variety of fish and invertebrate species and are used to derive a Final Acute Value. By taking into account the number and relative sensitivities of the tested species, the Final Acute Value is designed to protect most, but not necessarily all, of the tested and untested species.

Data on chronic toxicity to animals can be used to derive a Final Chronic Value by two different means. If chronic values are available for a specified number and array of species, a final chronic value can be calculated directly. If not, an acute-chronic ratio is derived and then used with the Final Acute Value to obtain the Final Chronic Value.

The Final Plant Value is obtained by selecting the lowest plant toxicity value based on measured concentrations.

The Final Residue Value is intended to protect wildlife which consume aquatic organisms and the marketability of aquatic organisms. Protection of the marketability of aquatic organisms is, in actuality, protection of a use of that water body ("commercial fishery"). Two kinds of data are necessary to calculate the Final Residue Value: a bioconcentration factor (BCF) and a maximum permissible tissue concentration, which can be an FDA action level or can be the result of a chronic wildlife feeding study. For lipid soluble pollutants, the BCF is normalized for percent lipids and then the Final Residue Value is calculated by dividing the maximum permissible tissue concentration by the normalized BCF and by an appropriate percent lipid value. BCFs are normalized for percent lipids since the BCF measured for any individual aquatic species is generally proportional to the percent lipids in that species.

If sufficient data are available to demonstrate that one or more of the final values should be related to a water quality characteristic, such as salinity, hardness, or suspended solids, the final value(s) are expressed as a function of that characteristic.

After the four final values (Final Acute Value, Final Chronic Value, Final Plant Value, and Final Residue Value) have been obtained, the criterion is established with the Final Acute Value becoming the maximum value and the lowest of the other three values becoming the 24-hour average value. All of the data used to calculate the four final values and any additional pertinent information are then reviewed to determine if the criterion is reasonable. If sound scientific evidence indicates that the criterion should be raised or lowered, appropriate changes are made as necessary.

The present Guidelines have been revised from the earlier published versions (43 FR 21506, May 18, 1978; 43 FR 29028, July 5, 1978; 44 FR 15926, March 15, 1979). Details have been added in many places and the concept of a minimum data base has been incorporated. In addition, three adjustment factors and the species sensitivity factor have been deleted. These modifications were the result of the Agency's analysis of public comments and comments received from the Science Advisory Board on earlier

versions of the Guidelines. These comments and the Resultant modifications are addressed fully in Appendix D to this notice.

Criteria for the Protection of Human Health

Interpretation of the Human Health Criteria

The human health criteria issued today are summarized in Appendix A of this **Federal Register** notice. Criteria for the protection of human health are presented for 62 of the 65 pollutants based on their carcinogenic, toxic, or organoleptic (taste and odor) properties. The meanings and practical uses of the criteria values are distinctly different depending on the properties on which they are based.

The objective of the health assessment portions of the criteria documents is to estimate ambient water concentrations which, in the case of non-carcinogens, prevent adverse health effects in humans, and in the case of suspect or proven carcinogens, represent various levels of incremental cancer risk.

Health assessments typically contain discussions of four elements: Exposure, pharmacokinetics, toxic effects, and criterion formulation.

The exposure section summarizes information on exposure routes: ingestion directly from water, indirectly from consumption of aquatic organisms found in ambient water, other dietary sources, inhalation, and dermal contact. Exposure assumptions are used to derive human health criteria. Most criteria are based solely on exposure from consumption of water containing a specified concentration of a toxic pollutant and through consumption of aquatic organisms which are assumed to have bioconcentrated pollutants from the water in which they live. Other multimedia routes of exposure such as air, non-aquatic diet, or dermal are not factored into the criterion formulation for the vast majority of pollutants due to lack of data. The criteria are calculated using the combined aquatic exposure pathway and also using the aquatic organism ingestion exposure route alone. In criteria reflecting both the water consumption and aquatic organism ingestion routes of exposure, the relative exposure contribution varies with the propensity of a pollutant to bioconcentrate, with the consumption of aquatic organisms becoming more important as the bioconcentration factor (BCF) increases. As additional information on total exposure is assembled for pollutants for which criteria reflect only the two specified aquatic exposure routes, adjustments in water concentration values may be made. The Agency intends to publish guidance which will permit the States to identify significantly different exposure patterns for their populations. If warranted by the demonstration of significantly different exposure patterns, this will become an element of a process to adapt/modify human health-based criteria to local conditions, somewhat analogous to the aquatic life criteria modification process discussed previously. It is anticipated that States at their discretion will be able to set appropriate human health criteria based on this process.

The pharmacokinetics section reviews data on absorption, distribution, metabolism, and excretion to assess the biochemical fate of the compounds in the human and animal system. The toxic effects section reviews data on acute, subacute, and chronic toxicity, synergistic and antagonistic effects, and specific information on mutagenicity, teratogenicity, and carcinogenicity. From this review, the toxic effect to be protected against is identified taking into account the quality, quantity, and weight of evidence characteristic of the data. The criterion formulation section reviews the highlights of the text and specifies a rationale for criterion development and the mathematical derivation of the criterion number.

Within the limitations of time and resources, current published information of significance was incorporated into the human health assessments. Review articles and reports were used for data evaluation and synthesis. Scientific judgment was exercised in reviewing and evaluating the data in each criteria document and in identifying the adverse effects for which protective criteria were published.

Specific health-based criteria are developed only if a weight of evidence supports the occurrence of the toxic effect and if dose/response data exist from which criteria can be estimated.

Criteria for suspect or proven carcinogens are presented as concentrations in water associated with a range of incremental cancer risks to man. Criteria for non-carcinogens represent levels at which exposure to a single chemical is not anticipated to produce adverse effects in man. In a few cases, organoleptic (taste and odor) data form the basis for the criterion. While this type of criterion does not represent a value which directly affects human health, it is presented as an estimate of the level of a pollutant that will not produce unpleasant taste or odor either directly from water consumption or indirectly by consumption of aquatic organisms found in ambient waters. A criterion developed in this manner is judged to be as useful as other types of criteria in protecting designated water uses. In addition, where data are available, toxicity-based criteria are also presented for pollutants with derived organoleptic criteria. The choice of criteria used in water quality standards for these pollutants will depend upon the designated use to be protected. In the case of a multiple use water body, the criterion protecting the most sensitive use will be applied. Finally, for several pollutants no criteria are recommended due to a lack of information sufficient for quantitative criterion formulation.

Risk Extrapolation

Because methods do not now exist to establish the presence of a threshold for carcinogenic effects, EPA's policy is that there is no scientific basis for estimating "safe" levels for carcinogens. The criteria for carcinogens, therefore, state that the recommended concentration for maximum protection of human health is zero. In addition, the Agency has presented a range of concentrations corresponding to incremental cancer risks of 10^{-7} to 10^{-5} (one additional case of cancer in populations ranging from ten million to 100,000, respectively). Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

Summary of the Human Health Guidelines

The health assessments and corresponding criteria published today were derived based on *Guidelines and Methodology Used in the Preparation of Health Effect Assessment Chapters of the Consent Decree Water Criteria Documents* (the Guidelines) developed by EPA's Office of Reserch and Development. The estimation of health risks associated with human exposure to environmental pollutants requires predicting the effect of low doses for up to a lifetime in duration. A combination of epidemiological and animal dose/response data is considered the preferred basis for quantitative criterion derivation. The complete Guidelines are presented as Appendix C. Major issues associated with these Guidelines and responses to public comments are presented as Appendix E.

No-effect (non-carcinogen) or specified risk (carcinogen) concentrations were estimated by extrapolation from animal toxicity or

human epidemiology studies using the following basic exposure assumptions: a 70-kilogram male person (*Report of the Task Group on Reference Man*, International Commission for Radiation Protection, November 23, 1957) as the exposed individual; the average daily consumption of freshwater and estuarine fish and shellfish products equal to 6.5 grams/day; and the average ingestion of two liters/day of water (*Drinking Water and Health*, National Academy of Sciences, National Research Council, 1977). Criteria based on these assumptions are estimated to be protective of an adult male who experiences average exposure conditions.

Two basic methods were used to formulate health criteria, depending on whether the prominent adverse effect was cancer or other toxic manifestations. The following sections detail these methods.

Carcinogens

Extrapolation of cancer responses from high to low doses and subsequent risk estimation from animal data is performed using a linearized multi-stage model. This procedure is flexible enough to fit all monotonically-increasing dose response data, since it incorporates several adjustable parameters. The multi-stage model is a linear non-threshold model as was the "one-hit" model originally used in the proposed criteria documents. The linearized multi-stage model and its characteristics are described fully in Appendix C. The linear non-threshold concept has been endorsed by the four agencies in the Interagency Regulatory Liaison Group and is less likely to underestimate risk at the low doses typical of environmental exposure than other models that could be used. Because of the uncertainties associated with dose response, animal-to-human extrapolation and other unknown factors, because of the use of average exposure assumptions, and because of the serious public health consequences that could result if risk were underestimated, EPA believes that it is prudent to use conservative methods to estimate risk in the water quality criteria program. The linearized multistage model is more systematic and invokes fewer arbitrary assumptions than the "one-hit" procedure previously used.

It should be noted that extrapolation models provide estimates of risk since a varitey of assumptions are built into any model. Models using widely different assumptions may produce estimates ranging over several orders of magnitude. Since there is at present no way to demonstrate the scientific validity of any model, the use of risk extrapolation models is a subject of debate in the scientific community. However, risk extrapolation is generally recognized as the only tool available at this time for estimating the magnitude of health hazards associated with non-threshold toxicants and has been endorsed by numerous Federal agencies and scientific organizations, including EPA's Carcinogen Assessment Group, the National Academy of Sciences, and the Interagency Regulatory Liaison Group as a useful means of assessing the risks of exposure to various carcinogenic pollutants.

Non-Carcinogens

Health criteria based on toxic effects of pollutants other than carcinogenicity are estimates of concentrations which are not expected to produce adverse effects in humans. They are based upon Acceptable Daily Intake (ADI) levels and are generally derived using no-observed-adverse-effect-level (NOAEL) data from animal studies although human data are used wherever available. The ADI is calculated using safety factors to account for uncertainties inherent in extrapolation from animal to man. In accordance with the National Research Council recommendations (*Drinking Water and Health*, National Academy of Sciences, National Research Council, 1977), safety factors of 10, 100, or 1,000 are used depending on the quality and quantity of data. In some instances extrapolations are made from inhalation studies or limits to approximate a human response from ingestion using the Stokinger-Woodward model (Journal of American Water Works Association, 1958). Calculations of criteria from ADIs are made using the standard exposure assumptions (2 liters of water, 6.5 grams of edible aquatic products, and an average body weight of 70 kg).

Dated: October 24, 1980.

Douglas M. Costle,

Administrator.

Appendix A—Summary of Water Quality Criteria

Acenaphthene

Freshwater Aquatic Life

The available data for acenaphthene indicate that acute toxicity to freshwater aquatic life occurs at concentrations as low as 1,700 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of acenaphthene to sensitive freshwater aquatic animals but toxicity to freshwater algae occur at concentrations as low as 520 μg/l.

Saltwater Aquatic Life

The available data for acenaphthene indicate that acute and chronic toxicity to saltwater aquatic life occur at concentrations as low as 970 and 710 μg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested. Toxicity to algae occurs at concentrations as low as 500 μg/l.

Human Health

Sufficient data is not available for acenaphthene to derive a level which would protect against the potential toxicity of this compound. Using available organoleptic data, for controlling undesirable taste and odor quality of ambient water, the estimated level is 20 μg/l. It should be recognized that organoleptic data as a basis for establishing a water quality criteria have limitations and have no demonstrated relationship to potential adverse human health effects.

Acrolein

Freshwater Aquatic Life

The available data for acrolein indicate that acute and chronic toxicity to freshwater aquatic life occurs at concentrations as low as 68 and 21 μg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

Saltwater Aquatic Life

The available data for acrolein indicate that acute toxicity to saltwater aquatic life occurs at concentrations as low as 55 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of acrolein to sensitive saltwater aquatic life.

Human Health

For the protection of human health from the toxic properties of acrolein ingested through water and contaminated aquatic organisms, the ambient water criterion is determined to be 320 μg/l.

For the protection of human health from the toxic properties of acrolein ingested through contaminated aquatic organisms alone, the ambient water criterion is determined to be 780 μg/l.

Acrylonitrile

Freshwater Aquatic Life

The available data for acrylonitrile indicate that acute toxicity to freshwater aquatic life occurs at concentrations as

low as 7,550 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No definitive data are available concerning the chronic toxicity of acrylonitrile to sensitive freshwater aquatic life but mortality occurs at concentrations as low as 2,600 μg/l with a fish species exposed for 30 days.

Saltwater Aquatic Life

Only one saltwater species has been tested with acrylonitrile and no statement can be made concerning acute or chronic toxicity.

Human Health

For the maximum protection of human health from the potential carcinogenic effects due to exposure of acrylonitrile through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are .58 μg/l, .058 μg/l and .006 μg/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 6.5 μg/l, .65 μg/l, and .065 μg/l, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

Aldrin-Dieldrin

Dieldrin

Freshwater Aquatic Life

For dieldrin the criterion to protect fresh water aquatic life as derived using the Guidelines is 0.0019 μg/l as a 24-hour average and the concentration should not exceed 2.5 μg/l at any time.

Saltwater Aquatic Life

For dieldrin the criterion to protect saltwater aquatic life as derived using the Guidelines is 0.0019 μg/l as a 24-hour average and the concentration should not exceed 0.71 μg/l at any time.

Human Health

For the maximum protection of human health from the potential carcinogenic effects due to exposure of dieldrin through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are .71 ng/l, .071 ng/l, and .0071 ng/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are .76 ng/l, .076 ng/l, and .0076 ng/l respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

Aldrin

Freshwater Aquatic Life

For freshwater aquatic life the concentration of aldrin should not exceed 3.0 μg/l at any time. No data are available concerning the chronic toxicity of aldrin to sensitive freshwater aquatic life.

Saltwater Aquatic Life

For saltwater aquatic life the concentration of aldrin should not exceed 1.3 μg/l at any time. No data are available concerning the chronic toxicity of aldrin to sensitive saltwater aquatic life.

Human Health

For the maximum protection of human health from the potential carcinogenic effects due to exposure of aldrin through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are .74 ng/1, .074 ng/1, and .0074 ng/1, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are .79 ng/1, .079 ng/1, and .0079 ng/1, respectively. Other concentrations respresenting different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

Antimony

Freshwater Aquatic Life

The available data for antimony indicate that acute and chronic toxicity to freshwater aquatic life occur at concentrations as low as 9,000 and 1,600 μg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested. Toxicity to algae occurs at concentrations as low as 610 μg/l.

Saltwater Aquatic Life

No saltwater organisms have been adequately tested with antimony, and no statement can be made concerning acute or chronic toxicity.

Human Health

For the protection of human health from the toxic properties of antimony ingested through water and contaminated aquatic organisms, the ambient water criterion is determined to be 146 μg/l.

For the protection of human health from the toxic properties of antimony ingested through contaminated aquatic organisms alone, the ambient water criterion is determined to be 45,000 μg/l.

Arsenic

Freshwater Aquatic Life

For freshwater aquatic life the concentration of total recoverable trivalent inorganic arsenic should not exceed 440 μg/l at any time. Short-term effects on embryos and larvae of aquatic vertebrate species have been shown to occur at concentrations as low as 40 μg/l.

Saltwater Aquatic Life

The available data for total recoverable trivalent inorganic arsenic indicate that acute toxicity to saltwater aquatic life occurs at concentrations as low as 508 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of trivalent inorganic arsenic to sensitive saltwater aquatic life.

Human Health

For the maximum protection of human health from the potential carcinogenic effects due to exposure of arsenic through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are

estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are 22 ng/l, 2.2 ng/l, and .22 ng/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 175 ng/l, 17.5 ng/l, and 1.75 ng/l, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

Asbestos

Freshwater Aquatic Life

No freshwater organisms have been tested with any asbestiform mineral and no statement can be made concerning acute or chronic toxicity.

Saltwater Aquatic Life

No saltwater organisms have been tested with any asbestiform mineral and no statement can be made concerning acute or chronic toxicity.

Human Health

For the maximum protection of human health from the potential carcinogenic effects due to exposure of asbestos through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are 300,000 fibers/1,30,000 fibers/1, and 3,000 fibers/1, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

Benzene

Freshwater Aquatic Life

The available data for benzene indicate that acute toxicity to freshwater aquatic life occurs at concentrations as low as 5,300 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of benzene to sensitive freshwater aquatic life.

Saltwater Aquatic Life

The available data for benzene indicate that acute toxicity to saltwater aquatic life occurs at concentrations as low as 5,100 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No definitive data are available concerning the chronic toxicity of benzene to sensitive saltwater aquatic life, but adverse effects occur at concentrations as low as 700 μg/l with a fish species exposed for 168 days.

Human Health

For the maximum protection of human health from the potential carcinogenic effects due to exposure of benzene through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are 6.6 μg/l, .66 μg/l, and .066 μg/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 400 μg/l, 40.0 μg/l, and 4.0 μg/l, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

Benzidine

Freshwater Aquatic Life

The available data for benzidine indicate that acute toxicity to freshwater aquatic life occurs at concentrations as low as 2,500 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of benzidine to sensitive freshwater aquatic life.

Saltwater Aquatic Life

No saltwater organisms have been tested with benzidine and no statement can be made concerning acute and chronic toxicity.

Human Health

For the maximum protection of human health from the potential carcinogenic effects due to exposure of benzidine through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are 1.2 ng/1, .12 ng/1, and .01 ng/1, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 5.3 ng/1, .53 ng/1, and .05 ng/1, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

Beryllium

Freshwater Aquatic Life

The available data for beryllium indicate that acute and chronic toxicity to freshwater aquatic life occurs at concentrations as low as 130 and 5.3 μg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested. Hardness has a substantial effect on acute toxicity.

Salt water Aquatic Life

The limited saltwater data base available for beryllium does not permit any statement concerning acute or chronic toxicity.

Human Health

For the maximum protection of human health from the potential carcinogenic effects due to exposure of beryllium through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are 37 ng/l, 3.7 ng/l, and .37 ng/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 641 ng/l, 64.1 ng/l, and 6.41 ng/l, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

Cadmium

Freshwater Aquatic Life

For total recoverable cadmium the criterion (in μg/l) to protect freshwater aquatic life as derived using the Guidelines is the numerical value given

by $e^{[1.05\ [\ln(\text{hardness})]-3.53}$ as a 24-hour average and the concentration (in μg/l) should not exceed the numerical value given by $e^{[1.05\ [\ln(\text{hardness})]-3.73}$ at any time. For example, a hardnesses of 50, 100, and 200 mg/l as $CaCO_3$ the criteria are 0.012, 0.025, and 0.051 μg/l, respectively, and the concentration of total recoverable cadmium should not exceed 1.5, 3.0 and 6.3 μg/l, respectively, at any time.

Saltwater Aquatic Life

For total recoverable cadmium the criterion to protect saltwater aquatic life as derived using the Guidelines is 4.5 μg/l as a 24-hour average and the concentration should not exceed 59 μg/l at any time.

Human Health

The ambient water quality criterion for cadmium is recommended to be identical to the existing drinking water standard which is 10 μg/l. Analysis of the toxic effects data resulted in a calculated level which is protective of human health against the ingestion of contaminated water and contaminated aquatic organisms. The calculated value is comparable to the present standard. For this reason a selective criterion based on exposure solely from consumption of 6.5 grams of aquatic organisms was not derived.

Carbon Tetrachloride

Freshwater Aquatic Life

The available date for carbon tetrachloride indicate that acute toxicity to freshwater aquatic life occurs at concentrations as low as 35,200 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of carbon tetrachloride to sensitive freshwater aquatic life.

Saltwater Aquatic Life

The available data for carbon tetrachloride indicate that acute toxicity to saltwater aquatic life occurs at concentrations as low as 50,000 μg/l and would occur at lower concentrations among species that are more sensitive that those tested. No data are available concerning the chronic toxicity of carbon tetrachloride to sensitive saltwater aquatic life.

Human Health

For the maximum protection of human health from the potential carcinogenic effects due to exposure of carbon tetrachloride through ingestion of contaminated water and contaminated aquatic organisms the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are 4.0μg/l, .40 μg/l, and .04 μg/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 69.4 μg/l, 6.94 μg/l, and .69 μg/l, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

Chlordane

Freshwater Aquatic Life

For chlordane the criterion to protect freshwater aquatic life as derived using the Guidelines is 0.0043 μg/l as a 24-hour average and the concentration should not exceed 2.4 μg/l at any time.

Saltwater Aquatic Life

For chlordane the criterion to protect saltwater aquatic life as derived using the Guidelines is 0.0040 μg/l as a 24-hour average and the concentration should not exceed 0.09 μg/l at any time.

Human Health

For the maximum protection of human health from the potential carcinogenic effects due to exposure of chlordane through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are 4.6 ng/l, .46 ng/l, and .046 ng/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 4.8 ng/l, .48 ng/l, and .048 ng/l, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

Chlorinated Benzenes

Freshwater Aquatic Life

The available data for chlorinated benzenes indicate that acute toxicity to freshwater aquatic life occurs at concentrations as low as 250 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of the more toxic of the chlorinated benzenes to sensitive freshwater aquatic life but toxicity occurs at concentrations as low as 50 μg/l for a fish species exposed for 7.5 days.

Saltwater Aquatic Life

The available data for chlorinated benzenes indicate that acute and chronic toxicity to saltwater aquatic life occur at concentrations as low as 160 and 129 μg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

Human Health

For the maximum protection of human health from the potential carcinogenic effects due to exposure of hexachlorobenzene through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding recommended criteria are 7.2 ng/l, .72 ng/l, and .072 ng/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 7.4 ng/l, .74 ng/l, and .074 ng/l, respectively.

For the protection of human health from the toxic properties of 1,2,4,5-tetrachlorobenzene ingested through water and contaminated aquatic organisms, the ambient water criterion is determined to be 38 μg/l.

For the protection of human health from the toxic properties of 1,2,4,5-tetrachlorobenzene ingested through contaminated aquatic organisms alone, the ambient water criterion is determined to be 48 μg/l.

For the protection of human health from the toxic properties of pentachlorobenzene ingested through water and contaminated aquatic organisms, the ambient water criterion is determined to be 74 μg/l.

For the protection of human health from the toxic properties of pentachlorobenzene ingested through contaminated aquatic organisms alone, the ambient water criterion is determined to be 85 μg/l.

Using the present guidelines, a satisfactory criterion cannot be derived

at this time due to the insufficiency in the available data for trichlorobenzene.

For comparison purposes, two approaches were used to derive criterion levels for monochlorobenzene. Based on available toxicity data, for the protection of public health, the derived level is 488 μg/l. Using available organoleptic data, for controlling undesirable taste and odor quality of ambient water, the estimated level is 20 μg/l. It should be recognized that organoleptic data as a basis for establishing a water quality criteria have limitations and have no demonstrated relationship to potential adverse human health effects.

Chlorinated Ethanes

Freshwater Aquatic Life

The available freshwater data for chlorinated ethanes indicate that toxicity increases greatly with increasing chlorination, and that acute toxicity occurs at concentrations as low as 118,000 μg/l for 1,2-dichloroethane, 18,000 μg/l for two trichloroethanes, 9,320 μg/l for two tetrachloroethanes, 7,240 μg/l for pentachloroethane, and 980 μg/l for hexachloroethane. Chronic toxicity occurs at concentrations as low as 20,000 μg/l for 1,2-dichloroethane, 9,400 μg/l for 1,1,2-trichloroethane, 2,400 μg/l for 1,1,2,2,-tetrachloroethane, 1,100 μg/l for pentachloroethane, and 540 μg/l for hexachloroethane. Acute and chronic toxicity would occur at lower concentrations among species that are more sensitive than those tested.

Saltwater Aquatic Life

The available saltwater data for chlorinated ethanes indicate that toxicity increases greatly with increasing chlorination and that acute toxicity to fish and invertebrate species occurs at concentrations as low as 113,000 μg/l for 1,2-dichloroethane, 31,200 μg/l for 1,1,1-trichloroethane, 9,020 μg/l for 1,1,2,2-tetrachloroethane, 390 μg/l for pentachloroethane, and 940 μg/l for hexachloroethane. Chronic toxicity occurs at concentrations as low as 281 μg/l for pentachloroethane. Acute and chronic toxicity would occur at lower concentrations among species that are more sensitive than those tested.

Human Health

For the maximum protection of human health from the potential carcinogenic effects due to exposure of 1,2-dichloroethane through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are 9.4 μg/l, .94 μg/l, and .094 μg/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 2,430 μg/l, 243 μg/l, and 24.3 μg/l respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

For the protection of human health from the toxic properties of 1,1,1-trichloroethane ingested through water and contaminated aquatic organism, the ambient water criterion is determined to be 18.4 mg/l.

For the protection of human health from the toxic properties of 1,1,1,-trichloroethane ingested through contaminated aquatic organisms alone, the ambient water criterion is determined to be 1.03 g/l.

For the maximum protection of human health from the potential carcinogenic effects due to exposure of 1,1,2-trichloroethane through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are 6.0 μg/l, .6 μg/l, and .06 μg/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 418 μg/l, 41.8 μg/l, and 4.18 μg/l respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

For the maximum protection of human health from the potential carcinogenic effects due to exposure of 1,1,2,2-tetrachloroethane through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are 1.7 μg/l, .17 μg/l, and .017 μg/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 107 μg/l, 10.7 μg/l, and 1.07 μg/l, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

For the maximum protection of human health from the potential carcinogenic effects due to exposure of hexachloroethane through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are 19 μg/l, 1.9 μg/l, and .19 μg/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 87.4 μg/l, 8.74 μg/l, and .87 μg/l, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

Using the present guidelines, a satisfactory criterion cannot be derived at this time due to the insufficiency in the available data for monochloroethane.

Using the present guidelines, a satisfactory criterion cannot be derived at this time due to the insufficiency in the available data for 1,1,-dichloroethane.

Using the present guidelines, a satisfactory criterion cannot be derived at this time due to the insufficiency in the available data for 1,1,1,2-tetrachloroethane.

Using the present guidelines, a satisfactory criterion cannot be derived at this time due to the insufficiency in the available data for pentachloroethane.

Chlorinated Naphthalenes

Freshwater Aquatic Life

The available data for chlorinated naphthalenes indicate that acute toxicity to freshwater aquatic life occurs at concentrations as low as 1,600 μg/l and would occur at lower concentrations among species that are

more sensitive than those tested. No data are available concerning the chronic toxicity of chlorinated naphthalenes to sensitive freshwater aquatic life.

Saltwater Aquatic Life

The available data for chlorinated napthalenes indicate that acute toxicity to saltwater aquatic life occurs at concentrations as low as 7.5 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of chlorinated naphthalenes to sensitive saltwater aquatic life.

Human Health

Using the present guidelines, a satisfactory criterion cannot be derived at this time due to the insufficiency in the available data for chlorinated napthalenes.

Chlorinated Phenols

Freshwater Aquatic Life

The available freshwater data for chlorinated phenols indicate that toxicity generally increases with increasing chlorination, and that acute toxicity occurs at concentrations as low as 30 μg/l for 4-chloro-3-methylphenol to greater than 500,000 μg/l for other compounds. Chronic toxicity occurs at concentrations as low as 970 μg/l for 2,4,6-trichlorophenol. Acute and chronic toxicity would occur at lower concentrations among species that are more sensitive than those tested.

Saltwater Aquatic Life

The available saltwater data for chlorinated phenols indicate that toxicity generally increases with increasing chlorination and that acute toxicity occurs at concentrations as low as 440 μg/l for 2,3,5,6-tetrachlorophenol and 29,700 μg/l for 4-chlorophenol. Acute toxicity would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of chlorinated phenols to sensitive saltwater aquatic life.

Human Health

Sufficient data is not available for 3-nonochlorophenol to derive a level which would protect against the potential toxicity of this compound. Using available organoleptic data, for controlling undesirable taste and odor quality of ambient water, the estimated level is 0.1 μg/l. It should be recognized that organoleptic data as a basis for establishing a water quality criteria have limitations and have no demonstrated relationship to potential adverse human health effects.

Sufficient data is not available for 4-monochlorophenol to derive a level which would protect against the potential toxicity of this compound. Using available organoleptic data, for controlling undesirable taste and odor quality of ambient water, the estimated level is 0.1 μg/l. It should be recognized that organoleptic data as a basis for establishing a water quality criteria have limitations and have no demonstrated relationship to potential adverse human health effects.

Sufficient data is not available for 2,3-dichlorophenol to derive a level which would protect against the potential toxicity of this compound. Using available organoleptic data, for controlling undesirable taste and odor quality of ambient water, the estimated level is .04 μg/l. It should be recognized that organoleptic data as a basis for establishing a water quality criteria have limitations and have no demonstrated relationship to potential adverse human health effects.

Sufficient data is not available for 2,5-dichlorophenol to derive a level which would protect against the potential toxicity of this compound. Using available organoleptic data, for controlling undesirable taste and odor quality of ambient water, the estimated level is .5 μg/l. It should be recognized that organoleptic data as a basis for establishing a water quality criteria have limitations and have no demonstrated relationship to potential adverse human health effects.

Sufficient data is not available for 2,6-dichlorophenol to derive a level which would protect against the potential toxicity of this compound. Using available organoleptic data, for controlling undesirable taste and odor quality of ambient water, the estimated level is .2 μg/l. It should be recognized that organoleptic data as a basis for establishing a water quality criteria have limitations and have no demonstrated relationship to potential adverse human health effects.

Sufficient data is not available for 3,4-dichlorophenol to derive a level which would protect against the potential toxicity of this compound. Using available organoleptic data, for controlling undesirable taste and odor quality of ambient water, the estimated level is .3 μg/l. It should be recognized that organoleptic data as a basis for establishing a water quality criteria have limitations and have no demonstrated relationship to potential adverse human health effects.

Sufficient data is not available for 2,3,4,6-tetrachlorophenol to derive a level which would protect against the potential toxicity of this compound. Using available organoleptic data, for controlling undesirable taste and odor quality of ambient water, the estimated level is 1 μg/l. It should be recognized that organoleptic data as a basis for establishing a water quality criteria have limitations and have no demonstrated relationship to potential adverse human health effects.

For comparison purposes, two approaches were used to derive criterion levels for 2,4,5-trichlorophenol. Based on available toxicity data, for the protection of public health, the derived level is 2.6 mg/l. Using available organoleptic data, for controlling undesirable taste and odor quality of ambient water, the estimated level is 1.0 μg/l. It should be recognized that organoleptic data as a basis for establishing a water quality criteria have limitations and have no demonstrated relationship to potential adverse human health effects.

For the maximum protection of human health from the potential carcinogenic effects due to exposure of 2,4,6-trichlorophenol through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are 12 μg/l, 1.2 μg/l, and .12 μg/l respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 36 μg/l, 3.6 μg/l, and .36 μg/l, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

Using available organoleptic data, for controlling undesirable taste and odor quality of ambient water, the estimated level is 2 μg/l. It should be recognized that organoleptic data as a basis for establishing a water quality criterion have limitations and have no demonstrated relationship to potential adverse human health effects.

Sufficient data is not available for 2-methyl-4-chlorophenol to derive a level which would protect against any potential toxicity of this compound. Using available organoleptic data, for controlling undesirable taste and odor quality of ambient water, the estimated level is 1800 μg/l. It should be

recognized that organoleptic data as a basis for establishing a water quality criterion have limitations and have no demonstrated relationship to potential adverse human health effects.

Sufficient data is not available for 3-methyl-4-chlorophenol to derive a level which would protect against the potential toxicity of this compound. Using available organoleptic data, for controlling undesirable taste and odor quality of ambient water, the estimated level is 3000 μg/l. It should be recognized that organoleptic data as a basis for establishing a water quality criterion have limitations and have no demonstrated relationship to potential adverse human health effects.

Sufficient data is not available for 3-methyl-6-chlorophenol to derive a level which would protect against the potential toxicity of this compound. Using available organoleptic data, for controlling undesirable taste and odor quality of ambient water, the estimated level is 20 μg/l. It should be recognized that organoleptic data as a basis for establishing a water quality criterion have limitations and have no demonstrated relationship to potential adverse human health effects.

Chloroalkyl Ethers

Freshwater Aquatic Life

The available data for chloroalkyl ethers indicate that acute toxicity to freshwater aquatic life occurs at concentrations as low as 238,000 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No definitive data are available concerning the chronic toxicity of chloroalkyl ethers to sensitive freshwater aquatic life.

Saltwater Aquatic Life

No saltwater organisms have been tested with any chloroalkyl ether and no statement can be made concerning acute and chronic toxicity.

Human Health

For the maximum protection of human health from the potential carcinogenic effects due to exposure of bis-(chloromethyl)-ether through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are .038 ng/l, .0038 ng/l, and .00038 ng/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 18.4 ng/l, 1.84 ng/l, and .184 ng/l, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

For the maximum protection of human health from the potential carcinogenic effects due to exposure of bis (2-chloroethyl) ether through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are .3 μg/l, .03 μg/l, and .003 μg/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 13.6 μg/l, 1.36 μg/l, and .136 μg/l, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

For the protection of human health from the toxic properties of bis (2-chloroisopropyl) ether ingested through water and contaminated aquatic organisms, the ambient water criterion is determined to be 34.7 μg/l.

For the protection of human health from the toxic properties of bis (2-chloroisopropyl) ether ingested through contaminated aquatic organisms alone, the ambient water criterion is determined to be 4.36 mg/l.

Chloroform

Freshwater Aquatic Life

The available data for choloroform indicate that acute toxicity to freshwater aquatic life occurs at concentrations as low as 28,900 μg/l, and would occur at lower concentrations among species that are more sensitive than the three tested species. Twenty-seven-day LC50 values indicate that chronic toxicity occurs at concentrations as low as 1,240 μg/l, and could occur at lower concentrations among species or other life stages that are more sensitive than the earliest life cycle stage of the rainbow trout.

Saltwater Aquatic Life

The data base for saltwater species is limited to one test and no statement can be made concerning acute or chronic toxicity.

Human Health

For the maximum protection of human health from the potential carcinogenic effects due to exposure of chloroform through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are 1.90 μg/l, .19 μg/l, and .019 μg/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 157 μg/l, 15.7 μg/l, and 1.57 μg/l, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

2-Chlorophenol

Freshwater Aquatic Life

The availabe data for 2-chlorophenol indicate that acute toxicity to freshwater aquatic life occurs at concentrations as low as 4,380 μg/l and would occur at lower concentrations among species that are more sensitive that those tested. No definitive data are available concerning the chronic toxicity of 2-chlorophenol to sensitive freshwater aquatic life but flavor impairment occurs in one species of fish at concentrations as low as 2,000 μg/l.

Saltwater Aquatic Life

No saltwater organisms have been tested with 2-chlorophenol and no statement can be made concerning acute and chronic toxicity.

Human Health

Sufficient data is not available for 2-chlorophenol to derive a level which would protect against the potential toxicity of this compound. Using available organoleptic data, for controlling undesirable taste and odor quality of ambient water, the estimated level is 0.1 μg/l. It should be recognized that organoleptic data as a basis for establishing a water quality criteria have limitations and have no

demonstrated relationship to potential adverse human health effects.

Chromium

Freshwater Aquatic Life

For total recoverable hexavalent chromium the criterion to protect freshwater aquatic life as derived using the Guidelines is 0.29 μg/l as a 24-hour average and the concentration should not exceed 21 μg/l at any time.

For freshwater aquatic life the concentration (in μg/l) of total recoverable trivalent chromium should not exceed the numerical value given by "e[1.08[ln(hardness)]+3.48)" at any time. For example, at hardnesses of 50, 100 and 200 mg/l as $CaCO_3$ the concentration of total recoverable trivalent chromium should not exceed 2,200, 4,700, and 9,900 μg/l, respectively, at any time. The available data indicate that chronic toxicity to freshwater aquatic life occurs at concentrations as ow a 44 μg/l and would occur at lower :oncentrations among species that are nore sensitive than those tested.

Saltwater Aquatic Life

For total recoverable hexavalent hromium the criterion to protect altwater aquatic life as derived using he Guidelines is 18 μg/l as a 24-hour verage and the concentration should ot exceed 1,260 μg/l at any time.

For total recoverable trivalent hromium, the availabe data indicate iat acute toxicity to saltwater aquatic fe occurs at concentrations as low as 0,300 μg/l, and would occur at lower oncentrations amoung species that are iore sensitive than those tested. No ata are available concerning the ironic toxicity of trivalent chromium to ensitive saltwater aquatic life.

uman Health

For the protection of human health om the toxic properties of Chromium [ingested through water and – ntaminated aquatic organisms, the nbient water criterion is determined to : 170 mg/l.

For protection of human health om t oxic properties of Chromium ingested through contaminated uatic organisms alone, the ambient iter criterion is determined to be 3433 g/l.

The ambient water quality criterion total Chromium VI is recommended be identical to the existing drinking ter standard which is 50 μg/l. alysis of the toxic effects data ulted in a calculated level which is otective of human health against the estion of contaminated water and ntaminated aquatic organisms. The calculated value is comparable to the present standard. For this reason a selective criterion based on exposure solely from consumption of 6.5 grams of aquatic organisms was not derived.

Copper

Freshwater Aquatic Life

For total recoverable copper the criterion to protect freshwater aquatic life as derived using the Guidelines is 5.6 μg/l as a 24-hour average and the concentration (in μg/l) should not exceed the numerical value given by e(0.94[ln(hardness)]-1.23) at any time. For example, at hardnesses of 50, 100, and 200 mg/l $CaCO_3$ the concentration of total recoverable copper should not exceed 12, 22, and 43 μg/l at any time.

Saltwater Aquatic Life

For total recoverable copper the criterion to protect saltwater aquatic life as derived using the Guidelines is 4.0 μg/l as a 24-hour average and the concentration should not exceed 23 μg/l at any time.

Human Health

Sufficient data is not available for copper to derive a level which would protect against the potential toxicity of this compound. Using available organoleptic data, for controlling undesirable taste and odor quality of ambient water, the estimated level is 1 mg/l. It should be recognized that organoleptic data as a basis for establishing a water quality criteria have limitations and have no demonstrated relationship to potential adverse human health effects.

Cyanide

Freshwater Aquatic Life

For free cyanide (sum of cyanide present as HCN and CN^-, expressed as CN) the criterion to protect freshwater aquatic life as derived using the Guidelines is 3.5 μg/l as a 24-hour average and the concentration should not exceed 52 μg/l at any time.

Saltwater Aquatic Life

The available data for free cyanide (sum of cyanide present as HCN and CN^-, expressed as CN) indicate that acute toxicity to saltwater aquatic life occurs at concentrations as low as 30 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. If the acute-chronic ratio for saltwater organisms is similar to that for freshwater organisms, chronic toxicity would occur at concentrations as low as 2.0 μg/l for the tested species and at lower concentrations among species that are more sensitive than those tested.

Human Health

The ambient water quality criterion for cyanide is recommended to be identical to the existing drinking water standard which is 200 μg/l. Analysis of the toxic effects data resulted in a calculated level which is protective of human health against the ingestion of contaminated water and contaminated aquatic organisms. The calculated value is comparable to the present standard. For this reason a selective criterion based on exposure solely from consumption of 6.5 grams of aquatic organisms was not derived.

DDT and Metabolites

Freshwater Aquatic Life

DDT

For DDT and its metabolites the criterion to protect freshwater aquatic life as derived using the Guidelines is 0.0010 μg/l as a 24-hour average and the concentration should not exceed 1.1 μg/l at any time.

TDE

The available data for TDE indicate that acute toxicity to freshwater aquatic life occurs at concentrations as low as 0.6 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of TDE to sensitive freshwater aquatic life.

DDE

The available data for DDE indicate that acute toxicity to freshwater aquatic life occurs at concentrations as low as 1,050 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of DDE to sensitive freshwater aquatic life.

Saltwater Aquatic Life

DDT

For DDT and its metabolites the criterion to protect saltwater aquatic life as derived using the Guidelines is 0.0010 μg/l as a 24-hour average and the concentration should not exceed 0.13 μg/l at any time.

TDE

The available data for TDE indicate that acute toxicity to saltwater aquatic life occurs at concentrations as low as 3.6 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the

chronic toxicity of TDE to sensitive saltwater aquatic life.

DDE

The available data for DDE indicate that acute toxicity to saltwater aquatic life occurs at concentrations as low as 14 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of DDE to sensitive saltwater aquatic life.

Human Health

For the maximum protection of human health from the potential carcinogenic effects due to exposure of DDT through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are .24 ng/l, .024 ng/l, and .0024 ng/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are .24 ng/l, .024 ng/l, and .0024 ng/l, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment of an "acceptable" risk level.

Dichlorobenzenes

Freshwater Aquatic Life

The available data for dichlorobenzenes indicate that acute and chronic toxicity to freshwater aquatic life occurs at concentrations as low as 1,120 and 763 μg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

Saltwater Aquatic Life

The available data for dichlorobenzenes indicate that acute toxicity to saltwater aquatic life occurs at concentrations as low as 1,970 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of dichlorobenzenes to sensitive saltwater aquatic life.

Human Health

For the protection of human health from the toxic properties of dichlorobenzenes (all isomers) ingested through water and contaminated aquatic organisms, the ambient water criterion is determined to be 400 μg/l.

For the protection of human health from the toxic properties of dichlorobenzenes (all isomers) ingested through contaminated aquatic organisms alone, the ambient water criterion is determined to be 2.6 mg/l.

Dichlorobenzidines

Freshwater Aquatic Life

The data base available for dichlorobenzidines and freshwater organisms is limited to one test on bioconcentration of 3,3'-dichlorobenzidine and no statement can be made concerning acute or chronic toxicity.

Saltwater Aquatic Life

No saltwater organisms have been tested with any dichlorobenzidine and no statement can be made concerning acute or chronic toxicity.

Human Health

For the maximum protection of human health from the potential carcinogenic effects due to exposure of dichlorobenzidine through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero base on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are .103 μg/l, .0103 μg/l, and .00103 μg/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are .204 μg/l, .0204 μg/l, and .00204 μg/l, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

Dichloroethylenes

Freshwater Aquatic Life

The available data for dichloroethylenes indicate that acute toxicity to freshwater aquatic life occurs at concentrations as low as 11,600 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No definitive data are available concerning the chronic toxicity of dichlorethylenes to sensitive freshwater aquatic life.

Saltwater Aquatic Life

The available data for dichlorethylenes indicate that acute toxicity to saltwater aquatic life occurs at concentrations as low as 224,000 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity dichloroethylenes to sensitive saltwater aquatic life.

Human Health

For the maximum protection of human health from the potential carcinogenic effects due to exposure of 1,1-dichloroethylene through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are .33 μg/l, .033 μg/l, and .0033 μg/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 18.5 μg/l, 1.85 μg/l, and .185 μg/l, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

Using the present guidelines, a satisfactory criterion cannot be derived at this time due to the insufficency in the available data for 1,2-dichloroethylene.

2,4-Dichlorophenol

Freshwater Aquatic Life

The available data for 2,4-dichlorophenol indicate that acute and chronic toxicity to freshwater aquatic life occurs at concentrations as low as 2,020 and 365 μg/l, respectively, and would occur at lower concentrations among species that are more sensitive that those tested. Mortality to early life stages of one species of fish occurs at concentrations as low as 70 μg/l.

Saltwater Aquatic Life

Only one test has been conducted with saltwater organisms on 2,4-dichlorophenol and no statement can be made concerning acute or chronic toxicity.

Human Health

For comparison purposes, two approaches were used to derive criterion levels for 2,4-dichlorophenol.

Based on available toxicity data, for the protection of public health, the derived level is 3.09 mg/l. Using available organoleptic data, for controlling undesirable taste and odor quality of ambient water, the estimated level is 0.3 μg/l. It should be recognized that organoleptic data as a basis for establishing a water quality criteria have limitations and have no demonstrated relationship to potential adverse human health effects.

Dichloropropanes/Dichloropropenes

Freshwater Aquatic Life

The available data for dichloropropanes indicate that acute and chronic toxicity to freshwater aquatic life occurs at concentrations as low as 23,000 and 5,700 μg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

The available data for dichloropropenes indicate that acute and chronic toxicity to freshwater aquatic life occurs at concentrations as low as 6,060 and 244 μg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

Saltwater Aquatic Life

The available data for dichloropropanes indicate that acute and chronic toxicity to saltwater aquatic life occurs at concentrations as low as 10,300 and 3,040 μg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

The available data for dichloropropenes indicate that acute toxicity to saltwater aquatic life occurs at concentrations as low a as 790 μg/l, and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of dichloropropenes to sensitive saltwater aquatic life.

Human Health

Using the present guidelines, a satisfactory criterion cannot be derived at this time due to the insufficiency in the available data for dichloropropanes.

For the protection of human health from the toxic properties of dichloropropenes ingested through water and contaminated aquatic organisms, the ambient water criterion is determined to be 87 μg/l.

For the protection of human health from the toxic properties of dichloropropenes ingested through contaminated aquatic organisms alone, the ambient water criterion is determined to be 14.1 mg/l.

2,4-Dimethylphenol

Freshwater Aquatic Life

The available data for 2,4-dimethylphenol indicate that acute toxicity to freshwater aquatic life occurs at concentrations as low as 2,120 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of dimethylphenol to sensitive freshwater aquatic life.

Saltwater Aquatic Life

No saltwater organisms have been tested with 2,4-dimethylphenol and no statement can be made concerning acute and chronic toxicity.

Human Health

Sufficient data are not available for 2,4-dimethylphenol to derive a level which would protect against the potential toxicity of this compound. Using available organoleptic data, for controlling undersirable taste and odor quality of ambient water, the estimated level is 400 μg/l. It should be recognized that organoleptic data as a basis for establishing a water quality criteria have limitations and have no demonstrated relationship to potential adverse human health effects.

2,4-Dinitrotoluene

Freshwater Aquatic Life

The available data for 2,4-dinitrotoluene indicate that acute and chronic toxicity to freshwater aquatic life occurs at concentrations as low as 330 and 230 μg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

Saltwater Aquatic Life

The available data for 2,4-dinitrotoluenes indicate that acute toxicity to saltwater aquatic life occurs at concentrations as low as 590 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of 2,4-dinitrotoluenes to sensitive saltwater aquatic life but a decrease in algal cell numbers occurs at concentrations as low as 370 μg/l.

Human Health

For the maximum protection of human health from the potential carcinogenic effects due to exposure of 2,4-dinitrotoluene through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are 1.1 μg/l, 0.11 μg/l, and 0.011 μg/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 91 μg/l, 9.1 μg/l, and 0.91 μg/l, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

1,2-Diphenylhydrazine

Freshwater Aquatic Life

The available data for 1,2-diphenylhydrazine indicate that acute toxicity to freshwater aquatic life occurs at concentrations as low as 270 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of 1,2-diphenylhydrazine to sensitive freshwater aquatic life.

Saltwater Aquatic Life

No saltwater organisms have been tested with 1,2-diphenylhydrazine and no statement can be made concerning acute and chronic toxicity.

Human Health

For the maximum protection of human health from the potential carcinogenic effects due to exposure of 1,2-diphenylhydrazine through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are 422 ng/l, 42 ng/l, and 4 ng/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 5.6 μg/l, 0.56 μg/l, and 0.056 μg/l, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not

represent an Agency judgment on an "acceptable" risk level.

Endosulfan

Freshwater Aquatic Life

For endosulfan the criterion to protect freshwater aquatic life as derived using the Guidelines is 0.056 μg/l as a 24-hour average and the concentration should not exceed 0.22 μg/l at any time.

Saltwater Aquatic Life

For endosulfan the criterion to protect saltwater aquatic life as derived using the Guidelines is 0.0087 μg/l as a 24-hour average and the concentration should not exceed 0.034 μg/l at any time.

Human Health

For the protection of human health from the toxic properties of endosulfan ingested through water and contaminated aquatic organisms, the ambient water criterion is determined to be 74 μg/l.

For the protection of human health from the toxic properties of endosulfan ingested through contaminated aquatic organisms alone, the ambient water criterion is determined to be 159 μg/l.

Endrin

Freshwater Aquatic Life

For endrin the criterion to protect freshwater aquatic life as derived using the Guidelines is 0.0023 μg/l as a 24-hour average and the concentration should not exceed 0.18 μg/l at any time.

Saltwater Aquatic Life

For endrin the criterion to protect saltwater aquatic life as derived using the Guidelines is 0.0023 μg/l as a 24-hour average and the concentration should not exceed 0.037 μg/l at any time.

Human Health

The ambient water quality criterion for endrin is recommended to be identical to the existing drinking water standard which is 1 μg/l. Analysis of the toxic effects data resulted in a calculated level which is protective of human health against the ingestion of contaminated water and contaminated aquatic organisms. The calculated value is comparable to the present standard. For this reason a selective criterion based on exposure solely from consumption of 6.5 grams of aquatic organisms was not derived.

Ethylbenzene

Freshwater Aquatic Life

The available data for ethylbenzene indicate that acute toxicity to freshwater aquatic life occurs at concentrations as low as 32,000 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No definitive data are available concerning the chronic toxicity of ethylbenzene to sensitive freshwater aquatic life.

Saltwater Aquatic Life

The available data for ethylbenzene indicate that acute toxicity to saltwater aquatic life occurs at concentrations as low as 430 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of ethylbenzene to sensitive saltwater aquatic life.

Human Health

For the protection of human health from the toxic properties of ethylbenzene ingested through water and contaminated aquatic organisms, the ambient water criterion is determined to be 1.4 mg/l.

For the protection of human health from the toxic properties of ethylbenzene ingested through contaminated aquatic organisms alone, the ambient water criterion is determined to be 3.28 mg/l.

Fluoranthene

Freshwater Aquatic Life

The available data for fluoranthene indicate that acute toxicity to freshwater aquatic life occurs at concentrations as low as 3980 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of fluoranthene to sensitive freshwater aquatic life.

Saltwater Aquatic Life

The available data for fluoranthene indicate that acute and chronic toxicity to saltwater aquatic life occur at concentrations as low as 40 and 16 μg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

Human Health

For the protection of human health from the toxic properties of fluoranthene ingested through water and contaminated aquatic organisms, the ambient water criterion is determined to be 42 μg/l.

For the protection of human health from the toxic properties of fluoranthene ingested through contaminated aquatic organisms alone, the ambient water criterion is determined to be 54 μg/l.

Haloethers

Freshwater Aquatic Life

The available data for haloethers indicate that acute and chronic toxicity to freshwater aquatic life occur at concentrations as low as 360 and 122 μg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

Saltwater Aquatic Life

No saltwater organisms have been tested with any haloether and no statement can be made concerning acute or chronic toxicity.

Human Health

Using the present guidelines, a satisfactory criterion cannot be derived at this time due to the insufficiency in the available data for haloethers.

Halomethanes

Freshwater Aquatic Life

The available data for halomethanes indicate that acute toxicity to freshwater aquatic life occurs at concentrations as low as 11,000 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of halomethanes to sensitive freshwater aquatic life.

Saltwater Aquatic Life

The available data for halomethanes indicate that acute and chronic toxicity to saltwater aquatic life occur at concentrations as low as 12,000 and 6,400 μg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested. A decrease in algal cell numbers occurs at concentrations as low as 11,500 μg/l.

Human Health

For the maximum protection of human health from the potential carcinogenic effects due to exposure of chloromethane, bromomethane, dichloromethane, bromodichloromethane, tribromomethane, dichlorodifluoromethane, trichlorofluoromethane, or combinations of these chemicals through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk, over the lifetimes are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are

1.9 μg/l, 0.19 μg/l, and 0.019 μg/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 157 μg/l, 15.7 μg/l, and 1.57 μg/l, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

Heptachlor

Freshwater Aquatic Life

For heptachlor the criterion to protect freshwater aquatic life as derived using the Guidelines is 0.0038 μg/l as a 24-hour average and the concentration should not exceed 0.52 μg/l at any time.

Saltwater Aquatic Life

For heptachlor the criterion to protect saltwater aquatic life as derived using the Guidelines is 0.0036 μg/l as a 24-hour average and the concentration should not exceed 0.053 μg/l at any time.

Human Health

For the maximum protection of human health from the potential carcinogenic effects due to exposure of heptachlor through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk, over the lifetimes are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are 2.78 ng/l, .28 ng/l, and .028 ng/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 2.85 ng/l, .29 ng/l, and .029 ng/l, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

Hexachlorobutadiene

Freshwater Aquatic Life

The available data for hexachlorobutadiene indicate that acute and chronic toxicity to freshwater aquatic life occur at concentrations as low as 90 and 9.3 μg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

Saltwater Aquatic Life

The available data for hexachlorobutadiene indicate that acute toxicity to saltwater aquatic life occurs at concentrations as low as 32 μg/l and would occur at lower concentrations among species that are more sensitive that those tested. No data are available concerning the chronic toxicity of hexachlorobutadiene to sensitive saltwater aquatic life

Human Health

For the maximum protection of human health from the potential carcinogenic effects due to exposure of hexachlorobutadiene through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk, over the lifetimes are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are 4.47 μg/l, 0.45 μg/l, and 0.045 μg/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 500 μg/l, 50 μg/l, and 5 μg/l respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

Hexachlorocyclohexane

Lindane

Freshwater Aquatic Life

For Lindane the criterion to protect freshwater aquatic life as derived using the Guidelines is 0.080 μg/l as a 24-hour average and the concentration should not exceed 2.0 μg/l at any time.

Saltwater Aquatic Life

For saltwater aquatic life the concentration of lindane should not exceed 0.16 μg/l at any time. No data are available concerning the chronic toxicity of lindane to sensitive saltwater aquatic life.

BHC

Freshwater Aquatic Life

The available date for a mixture of isomers of BHC indicate that acute toxicity to freshwater aquatic life occurs at concentrations as low as 100 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of a mixture of isomers of BHC to sensitive freshwater aquatic life.

Saltwater Aquatic Life

The available date for a mixture of isomers of BHC indicate that acute toxicity to saltwater aquatic life occurs at concentrations as low as 0.34 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of a mixture of isomers of BHC to sensitive saltwater aquatic life.

Human Health

For the maximum protection of human health from the potential carcinogenic effects due to exposure of alpha-HCH through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk, over the lifetimes are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are 92 ng/l, 9.2 ng/l, and .92 ng/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 310 ng/l, 31.0 ng/l, and 3.1 ng/l respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

For the maximum protection of human health from the potential carcinogenic effects due to exposure of beta-HCH through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk, over the lifetimes are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are 163 ng/l, 16.3 ng/l, and 1.63 ng/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 547 ng/l, 54.7 ng/l, and 5.47 ng/l, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not

represent an Agency judgment on an "acceptable" risk level.

For the maximum protection of human health from the potential carcinogenic effects due to exposure of tech-HCH through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk, over the lifetimes are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are 123 ng/l, 12.3 ng/l, and 1.23 ng/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 414 ng/l, 41.4 ng/l, and 4.14 ng/l, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

For the maximum protection of human health from the potential carcinogenic effects due to exposure of gamma-HCH through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentrations should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are 186 ng/l, 18.6 ng/l, and 1.86 ng/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 625 ng/l, 62.5 ng/l, 6.25 ng/l, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

Using the present guidelines, a satisfactory criterion cannot be derived at this time due to the insufficiency in the available data for delta-HCH.

Using the present guidelines, a satisfactory criterion cannot be derived at this time due to the insufficiency in the available data for epsilon-HCH.

Hexachlorocyclopentadiene

Freshwater Aquatic Life

The available data for hexachlorocyclopentadiene indicate that acute and chronic toxicity to freshwater aquatic life occurs at concentrations as low as 7.0 and 5.2 μg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

Saltwater Aquatic Life

The available data to hexachlorocyclopentadiene indicate that acute toxicity to saltwater aquatic life occurs at concentrations as low as 7.0 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of hexachlorocyclopentadiene to sensitive saltwater aquatic life.

Human Health

For comparison purposes, two approaches were used to derive criterion levels for hexachlorocyclopentadiene. Based on available toxicity data, for the protection of public health, the derived level is 206 μg/l. Using available organoleptic data, for controlling undesirable taste and odor quality of ambient water, the estimated level is 1.0 μg/l. It should be recognized that organoleptic data as a basis for establishing a water quality criterion have limitations and have no demonstrated relationship to potential adverse human health effects.

Isophorone

Freshwater Aquatic Life

The available data for isophorone indicate that acute toxicity to freshwater aquatic life ocurs at concentrations as low as 117,000 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of isophorone to sensitive freshwater aquatic life.

Saltwater Aquatic Life

The available data for isophorone indicate that acute toxicity to saltwater aquatic life occurs at concentrations as low as 12,900 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of isophorone to sensitive saltwater aquatic life.

Human Health

For the protection of human health from the toxic properties of isophorone ingested through water and contaminated aquatic organisms, the ambient water criterion is determined to be 5.2 mg/l.

For the protection of human health from the toxic properties of isophorone ingested through contaminated aquatic organisms alone, the ambient water criterion is determined to be 520 mg/l.

Lead

Freshwater Aquatic Life

For total recoverable lead the criterion (in μg/l) to protect freshwater aquatic life as derived using the Guidelines is the numerical value given by e{2.35[ln(hardness)]-9.48} as a 24-hour average and the concentration (in μg/l) should not exceed the numerical value given by e{1.22[ln(hardness)]-0.47} at any time. For example, at hardnesses of 50, 100, and 200 mg/l as $CaCO_3$ the criteria are 0.75, 3.8, and 20 μg/l, respectively, as 24-hour averages, and the concentrations should not exceed 74, 170, and 400 μg/l, respectively, at any time.

Saltwater Aquatic Life

The available data for total recoverable lead indicate that acute and chronic toxicity to saltwater aquatic life occur at concentrations as low as 666 and 25 μg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

Human Health

The ambient water quality criterion for lead is recommended to be identical to the existing drinking water standard which is 50 μg/l. Analysis of the toxic effects data resulted in a calculated level which is protective to human health against the ingestion of contaminated water and contaminated aquatic organisms. The calculated value is comparable to the present standard. For this reason a selective criterion based on exposure solely from consumption of 6.5 grams of aquatic organisms was not derived.

Mercury

Freshwater Aquatic Life

For total recoverable mercury the criterion to protect freshwater aquatic life as derived using the Guidelines is 0.00057 μg/l as a 24-hour average and the concentration should not exceed 0.0017 μg/l at any time.

Saltwater Aquatic Life

For total recoverable mercury the criterion to protect saltwater aquatic life as derived using the Guidelines is 0.025 μg/l as a 24-hour average and the concentration should not exceed 3.7 μg/l at any time.

Human Health

For the protection of human health from the toxic properties of mercury

ingested through water and contaminated aquatic organisms, the ambient water criterion is determined to be 144 ng/l.

For the protection of human health from the toxic properties of mercury ingested through contaminated aquatic organisms alone, the ambient water criterion is determined to be 146 ng/l.

Note.—These values include the consumption of freshwater, estuarine, and marine species.

Naphthalene

Freshwater Aquatic Life

The available data to naphthalene indicate that acute and chronic toxicity to freshwater aquatic life occur at concentrations as low as 2,300 and 620 μg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

Saltwater Aquatic Life

The available data for naphthalene indicate that acute toxicity to saltwater aquatic life occurs at concentrations as low as 2,350 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of naphthalene to sensitive saltwater aquatic life.

Human Health

Using the present guidelines, a satisfactory criterion cannot be derived at this time due to the insufficiency in the available data for naphthalene.

Nickel

Freshwater Aquatic Life

For total recoverable nickel the criterion (in μg/l) to protect freshwater aquatic life as derived using the guidelines is the numerical value given by e(0.76 [ln (hardness)] +1.06) as a 24-hour average and the concentration (in μg/l) should not exceed the numerical value given by e(0.76[ln (hardness)] + 0.02) at any time. For example, at hardnesses of 50, 100, and 200 mg/l as $CaCO_3$ the criteria are 56, 96, and 160 μg/l, respectively, as 24-hour averages, and the concentrations should not exceed 1,100, 1,800, and 3,100 μg/l, respectively, at any time.

Saltwater Aquatic Life

For total recoverable nickel the criterion to protect saltwater aquatic life derived using the Guidelines is 7.1 μg/l as a 24-hour average and the concentration should not exceed 140 μg/l at any time.

Human Health

For the protection of human health from the toxic properties of nickel ingested through water and contaminated aquatic organisms, the ambient water criterion is determined to be 13.4 μg/l.

For the protection of human health from the toxic properties of nickel ingested through contaminated aquatic organisms alone, the ambient water criterion is determined to be 100 μg/l.

Nitrobenzene

Freshwater Aquatic Life

The available data for nitrobenzene indicate that acute toxicity to freshwater aquatic life occurs at concentrations as low as 27,000 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No definitive data are available concerning the chronic toxicity of nitrobenzene to sensitive freshwater aquatic life.

Saltwater Aquatic Life

The available data for nitrobenzene indicate that acute toxicity to saltwater aquatic life occurs at concentrations as low as 6,680 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of nitrobenzene to sensitive saltwater aquatic life.

Human Health

For comparison purposes, two approaches were used to derive criterion levels for nitrobenzene. Based on available toxicity data, for the protection of public health, the derived level is 19.8 mg/l. Using available organoleptic data, for controlling undesirable taste and odor quality of ambient water, the estimated level is 30 μg/l. It should be recognized that organoleptic data as a basis for establishing a water quality criteria have limitations and have no demonstrated relationship to potential adverse human health effects.

Nitrophenols

Freshwater Aquatic Life

The available data for nitrophenols indicate that acute toxicity to freshwater aquatic life occurs at concentrations as low as 230 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of nitrophenols to sensitive freshwater aquatic life but toxicity to one species of algae occurs at concentrations as low as 150 μg/l.

Saltwater Aquatic Life

The available data for nitrophenols indicate that acute toxicity to saltwater aquatic life occurs at concentrations as low as 4,850 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of nitrophenols to sensitive saltwater aquatic life.

Human Health

For the protection of human health from the toxic properties of 2,4-dinitro-o-cresol ingested through water and contaminated aquatic organisms, the ambient water criterion is determined to be 13.4 μg/l.

For the protection of human health from the toxic properties of 2,4-dinitro-o-cresol ingested through contaminated aquatic organisms alone, the ambient water criterion is determined to be 765 μg/l.

For the protection of human health from the toxic properties of dinitrophenol ingested through water and contaminated aquatic organisms, the ambient water criterion is determined to be 70 μg/l.

For the protection of human health from the toxic properties of dinitrophenol ingested through contaminated aquatic organisms alone, the ambient water criterion is determined to be 14.3 mg/l.

Using the present guidelines, a satisfactory criterion cannot be derived at this time due to the insufficiency in the available data for mononitrophenol.

Using the present guidelines, a satisfactory criterion cannot be derived at this time due to the insufficiency in the available data for tri-nitrophenol.

Nitrosamines

Freshwater Aquatic Life

The available data for nitrosamines indicate that acute toxicity to freshwater aquatic life occurs at concentrations as low as 5,850 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of nitrosamines to sensitive freshwater aquatic life.

Saltwater Aquatic Life

The available data for nitrosamines indicate that acute toxicity to saltwater aquatic life occurs at concentrations as low as 3,300,000 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of nitrosamines to sensitive saltwater aquatic life.

Human Health

For the maximum protection of human health from the potential carcinogenic effects due to exposure of n-nitrosodimethylamine through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk, over the lifetimes are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are 14 ng/l, 1.4 ng/l, and .14 ng/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 160,000 ng/l, 16,000 ng/l, and 1,600 ng/l, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

For the maximum protection of human health from the potential carcinogenic effects due to exposure of n-nitrosodiethylamine through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk, over the lifetimes are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are 8 ng/l, 0.8 ng/l, and 0.08 ng/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 12,400 ng/l, 1,240 ng/l, and 124 ng/l, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

For the maximum protection of human health from the potential carcinogenic effects due to exposure in n-nitrosodi-n-butylamine through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk, over the lifetimes are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are 64 ng/l 6.4 ng/l and .064 ng/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 5,868 ng/l, 587 ng/l, and 58.7 ng/l, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

For the maximum protection of human health from the potential carcinogenic effects due to exposure in n-nitrosodiphenylamine through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk, over the lifetimes are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are 49,000 ng/l 4,900 ng/l and 490 ng/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 161,000 ng/l, 16,100 ng/l, and 1,610 ng/l, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

For the maximum protection of human health from the potential carcinogenic effects due to exposure in n-nitrosopyrrolidine through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk, over the lifetimes are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are 160 ng/l 16.0 ng/l and 1.60 ng/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 919,000 ng/l, 91,900 ng/l, and 9,190 ng/l, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

Pentachlorophenol

Freshwater Aquatic Life

The available data for pentachlorophenol indicate that acute and chronic toxicity to freshwater aquatic life occur at concentrations as low as 55 and 3.2 μg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

Saltwater Aquatic Life

The available data for pentachlorophenol indicate that acute and chronic toxicity to saltwater aquatic life occur at concentrations as low as 53 and 34 μg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

Human Health

For comparison purposes, two approaches were used to derive criterion levels for pentachlorophenol. Based on available toxicity data, for the protection of public health, the derived level is 1.01 mg/l. Using available organoleptic data, for controlling undesirable taste and odor quality of ambient water, the estimated level is 30 μg/l. It should be recognized that organoleptic data as a basis for establishing a water quality criterion have limitations and have no demonstrated relationship to potential adverse human health effects.

Phenol

Freshwater Aquatic Life

The available data for phenol indicate that acute and chronic toxicity to freshwater aquatic life occur at concentrations as low as 10,200 and 2,560 μg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

Saltwater Aquatic Life

The available data for phenol indicate that acute toxicity to saltwater aquatic life occurs at concentrations as low as 5,800 ug/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of phenol to sensitive saltwater aquatic life.

Human Health

For comparison purposes, two approaches were used to derive criterion levels for phenol. Based on available toxicity data, for the protection of public health, the derived level is 3.5 mg/l. Using available organoleptic data, for controlling

undesirable taste and odor quality of ambient water, the estimated level is 0.3 mg/l. It should be recognized that organoleptic data as a basis for establishing a water quality criterion have limitations and have no demonstrated relationship to potential adverse human health effects.

Phthalate Esters

Freshwater Aquatic Life

The available data for phthalate esters indicate that acute and chronic toxicity to freshwater aquatic life occur at concentrations as low as 940 and 3 μg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

Saltwater Aquatic Life

The available data for phthalate esters indicate that acute toxicity to saltwater aquatic life occurs at concentrations as low as 2944 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of phthalate esters to sensitive saltwater aquatic life but toxicity to one species of algae occurs at concentrations as low as 3.4 μg/l.

Human Health

For the protection of human health from the toxic properties of dimethyl-phthalate ingested through water and contaminated aquatic organisms, the ambient water criterion is determined to be 313 mg/l.

For the protection of human health from the toxic properties of dimethyl-phthalate ingested through contaminated aquatic organisms alone, the ambient water criterion is determined to be 2.9 g/l.

For the protection of human health from the toxic properties of diethyl-phthalate ingested through water and contaminated aquatic organisms, the ambient water criterion is determined to be 350 mg/l.

For the protection of human health from the toxic properties of diethyl-phthalate ingested through contaminated aquatic organisms alone, the ambient water criterion is determined to be 1.8 g/l.

For the protection of human health from the toxic properties of dibutyl-phthalate ingested through water and contaminated aquatic organisms, the ambient water criterion is determined to be 34 mg/l.

For the protection of human health from the toxic properties of dibutyl-phthalate ingested through contaminated aquatic organisms alone, the ambient water criterion is determined to be 154 mg/l.

For the protection of human health from the toxic properties of di-2-ethylhexyl-phthalate ingested through water and contaminated aquatic organisms, the ambient water criterion is determined to be 15 mg/l.

For the protection of human health from the toxic properties of di-2-ethylhexyl-phthalate ingested through contaminated aquatic organisms alone, the ambient water criterion is determined to be 50 mg/l.

Polychlorinated Biphenyls

Freshwater Aquatic Life

For polychlorinated biphenyls the criterion to protect freshwater aquatic life as derived using the Guidelines is 0.014 μg/l as a 24-hour average. The available data indicate that acute toxicity to freshwater aquatic life probably will only occur at concentrations above 2.0 μg/l and that the 24-hour average should provide adequate protection against acute toxicity.

Saltwater Aquatic Live

For polychlorinated biphenyls the criterion to protect saltwater aquatic life as derived using the Guidelines is 0.030 μg/l as a 24-hour average. The available data indicate that acute toxicity to saltwater aquatic life probably will only occur at concentrations above 10 μg/l and that the 24-hour average should provide adequate protection against acute toxicity.

Human Health

For the maximum protection of human health from the potential carcinogenic effects due to exposure of PCBs through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are .79 ng/l, 0.79 ng/l, and .0079 ng/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are .79 ng/l, .079 ng/l, and .0079 ng/l, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

Polynuclear Aromatic Hydrocarbons (PAHs)

Freshwater Aquatic Life

The limited freshwater data base available for polynuclear aromatic hydrocarbons, mostly from short-term bioconcentration studies with two compounds, does not permit a statement concerning acute or chronic toxicity.

Saltwater Aquatic Life

The available data for polynuclear aromatic hydrocarbons indicate that acute toxicity to saltwater aquatic life occurs at concentrations as low as 300 ug/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of polynuclear aromatic hydrocarbons to sensitive saltwater aquatic life.

Human Health

For the maximum protection of human health from the potential carcinogenic effects due to exposure of PAHs through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are 28 ng/l, 2.8 ng/l, and .28 ng/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 311 ng/l, 31.1 ng/l, and 3.11 ng/l, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

Selenium

Freshwater Aquatic Life

For total recoverable inorganic selenite the criterion to protect freshwater aquatic life as derived using the Guidelines is 35 μg/l as a 24-hour average and the concentration should not exceed 260 μg/l at any time.

The available data for inorganic selenate indicate that acute toxicity to freshwater aquatic life occurs at concentrations as low as 760 μg/l and would occur at lower concentrations among species that are more sensitive

than those tested. No data are available concerning the chronic toxicity of inorganic selenate to sensitive freshwater aquatic life.

Saltwater Aquatic Life

For total recoverable inorganic selenite the criterion to protect saltwater aquatic life as derived using the Guidelines is 54 μg/l as a 24-hour average and the concentration should not exceed 410 μg/l at any time.

No data are available concerning the toxicity of inorganic selenate to saltwater aquatic life.

Human Health

The ambient water quality criterion for selenium is recommended to be identical to the existing drinking water standard which is 10 μg/l. Analysis of the toxic effects data resulted in a calculated level which is protective of human health against the ingestion of contaminated water and contaminated aquatic organisms. The calculated value is comparable to the present standard. For this reason a selective criterion based on exposure solely from consumption of 6.5 grams of aquatic organisms was not derived.

Silver

Freshwater Aquatic Life

For freshwater aquatic life the concentration (in μg/l) of total recoverable silver should not exceed the numerical value given by "e[1.72(ln (hardness)-6.52)]" at any time. For example, at hardnesses of 50, 100, 200 mg/l as $CaCO_3$ the concentration of total recoverable silver should not exceed 1.2, 4.1, and 13 μg/l, respectively, at any time. The available data indicate that chronic toxicity to freshwater aquatic life may occur at concentrations as low as 0.12 μg/l.

Saltwater Aquatic Life

For saltwater aquatic life the concentration of total recoverable silver should not exceed 2.3 μg/l at any time. No data are available concerning the chronic toxicity of silver to sensitive saltwater aquatic life.

Human Health

The ambient water quality criterion for silver is recommended to be identical to the existing drinking water standard which is 50 μg/l. Analysis of the toxic effects data resulted in a calculated level which is protective of human health against the ingestion of contaminated water and contaminated aquatic organisms. The calculated value is comparable to the present standard. For this reason a selective criterion based on exposure solely from consumption of 6.5 grams of aquatic organisms was not derived.

Tetrachloroethylene

Freshwater Aquatic Life

The available data for tetrachloroethylene indicate that acute and chronic toxicity to freshwater aquatic life occur at concentrations as low as 5,280 and 840 μg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

Saltwater Aquatic Life

The available data for tetrachloroethylene indicate that acute and chronic toxicity to saltwater aquatic life occur at concentrations low as 10,200 and 450 μg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

Human Health

For the maximum protection of human health from the potential carcinogenic effects due to exposure of tetrachloroethylene through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are 8 μg/l, .8 μg/l, and .08 μg/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 88.5 μg/l, 8.85 μg/l, and .88 μg/l, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

Thallium

Freshwater Aquatic Life

The available data for thallium indicate that acute and chronic toxicity to freshwater aquatic life occur at concentrations as low as 1,400 and 40 μg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested. Toxicity to one species of fish occurs at concentrations as low as 20 μg/l after 2,600 hours of exposure.

Saltwater Aquatic Life

The available data for thallium indicate that acute toxicity to saltwater aquatic life occurs at concentrations as low as 2,130 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of thallium to sensitive saltwater aquatic life.

Human Health

For the protection of human health from the toxic properties of thallium ingested through water and contaminated aquatic organisms, the ambient water criterion is determined to be 13 μg/l.

For the protection of human health from the toxic properties of thallium ingested through contaminated aquatic organisms alone, the ambient water criterion is determined to be 48 μg/l.

Toluene

Freshwater Aquatic Life

The available data for toluene indicate that acute toxicity to freshwater aquatic life occurs at concentrations as low as 17,500 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of toluene to sensitive freshwater aquatic life.

Saltwater Aquatic Life

The available data for toluene indicate that acute and chronic toxicity to saltwater aquatic life occur at concentrations as low as 6,300 and 5,000 μg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

Human Health

For the protection of human health from the toxic properties of toluene ingested through water and contaminated aquatic organisms, the ambient water criterion is determined to be 14.3 mg/l.

For the protection of human health from the toxic properties of toluene ingested through contaminated aquatic organisms alone, the ambient water criterion is determined to be 424 mg/l.

Toxaphene

Freshwater Aquatic Life

For toxaphene the criterion to protect freshwater aquatic life as derived using the Guidelines is 0.013 μg/l as a 24-hour average and the concentration should not exceed 1.6 μg/l at any time.

Saltwater Aquatic Life

For saltwater aquatic life the concentration of toxaphene should not exceed 0.070 μg/l at any time. No data

are available concerning the chronic toxicity of toxaphene to sensitive saltwater aquatic life.

Human Health

For the maximum protection of human health from the potential carcinogenic effects due to exposure of toxaphene through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are estimated at 10^{-6}, 10^{-6}, and 10^{-7}. The corresponding criteria are 7.1 ng/l, .71 ng/l, and .07 ng/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 7.3 ng/l, .73 ng/l, and .07 ng/l, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

Trichloroethylene

Freshwater Aquatic Life

The available data for trichloroethylene indicate that acute toxicity to freshwater aquatic life occurs at concentrations as low as 45,000 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of trichloroethylene to sensitive freshwater aquatic life but adverse behavioral effects occurs to one species at concentrations as low as 21,900 μg/l.

Saltwater Aquatic Life

The available data for trichloroethylene indicate that acute toxicity to saltwater aquatic life occurs at concentrations as low as 2,000 μg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of trichloroethylene to sensitive saltwater aquatic life.

Human Health

For the maximum protection of human health from the potential carcinogenic effects due to exposure of trichloroethylene through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are 27 μg/l, 2.7 μg/l, and .27 μg/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 807 μg/l, 80.7 μg/l, and 8.07 μg/l, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

Vinyl Chloride

Freshwater Aquatic Life

No freshwater organisms have been tested with vinyl chloride and no statement can be made concerning acute or chronic toxicity.

Saltwater Aquatic Life

No saltwater organisms have been tested with vinyl chloride and no statement can be made concerning acute or chronic toxicity.

Human Health

For the maximum protection of human health from the potential carcinogenic effects due to exposure of vinyl chloride through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentration should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding criteria are 20 μg/l, 2.0 μg/l, and .2 μg/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 5,246 μg/l, 525 μg/l, and 52.5 μg/l, respectively. Other concentrations representing different risk levels may be calculated by use of the Guidelines. The risk estimate range is presented for information purposes and does not represent an Agency judgment on an "acceptable" risk level.

Zinc

Freshwater Aquatic Life

For total recoverable zinc the criterion to protect freshwater aquatic life as derived using the Guidelines is 47 μg/l as a 24-hour average and the concentration (in μg/l) should not exceed the numerical value given by $e^{(0.83[\ln(\text{hardness})] + 1.95)}$ at any time. For example, at hardnesses of 50, 100, and 200 mg/l as $CaCO_3$ the concentration of total recoverable zinc should not exceed 180, 320, and 570 μg/l at any time.

Saltwater Aquatic Life

For total recoverable zinc the criterion to protect saltwater aquatic life as derived using the Guidelines is 58 μg/l as a 24-hour average and the concentration should not exceed 170 μg/l at any time.

Human Health

Sufficient data is not available for zinc to derive a level which would protect against the potential toxicity of this compound. Using available organoleptic data, for controlling undesirable taste and odor quality of ambient water, the estimated level is 5 mg/l. It should be recognized that organoleptic data as a basis for establishing a water quality criteria have limitations and have not demonstrated relationship to potential adverse human health effects.

Appendix B—Guidelines for Deriving Water Quality Criteria for the Protection of Aquatic Life and Its Uses

Introduction

This version of the Guidelines provides clarifications, additional details, and technical and editorial changes in the last version published in the Federal Register [44 FR 15970 (March 15, 1979)]. This version incorporates changes resulting from comments on previous versions and from experience gained during U.S. EPA's use of the previous versions. Future versions of the Guidelines will incorporate new ideas and data as their usefulness is demonstrated.

Criteria may be expressed in several forms. The numerical form is commonly used, but descriptive and procedural forms can be used if numerical criteria are not possible or desirable. The purpose of these Guidelines is to describe an objective, internally consistent and appropriate way of deriving numerical water quality criteria for the protection of the uses of, as well as the presence of, aquatic organisms.

A numerical criterion might be thought of as an estimate of the highest concentration of a substance in water which does not present a significant risk to the aquatic organisms in the water and their uses. Thus the Guidelines are intended to derive criteria which will protect aquatic communities by protecting most of the species and their uses most of the time, but not

necessarily all of the species all of the time. Aquatic communities can tolerate some stress and occasional adverse effects on a few species, and so total protection of all of the species all of the time is not necessary. Rather, the Guidelines attempt to provide a reasonable and adequate amount of protection with only a small possibility of considerable overprotection or underprotection. Within these constraints, it seems appropriate to err on the side of overprotection.

The numerical aquatic life criteria derived using the Guidelines are expressed as two numbers, rather than the traditional one number, so that the criteria can more accurately reflect toxicological and practical realities. The combination of both a maximum value and a 24-hour average value is designed to provide adequate protection of aquatic life and its uses from acute and chronic toxicity to animals, toxicity to plants and bioconcentration by aquatic organisms without being as restrictive as a one-number criterion would have to be to provide the same amout of protection. The only way to assure the same degree of protection with a one-number criterion would be to use the 24-hour average as a concentration that is not to be exceeded at any time in any place.

The two-number criterion is intended to identify an average pollutant concentration which will produce a water qualtiy generally suited to the maintenance of aquatic life and its uses while restricting the extent and duration of excursions over the average so that the total exposure will not cause unacceptable adverse effects. Merely specifying an average value over a time period is insufficient, unless the period of time is rather short, because of concentration higher than the average value can kill or cause substantial damage in short periods. Furthermore, for some substances the effect of intermittent high exposures is cumulative. It is therefore necessary to place an upper limit on pollutant concentrations to which aquatic organisms might be exposed, especially when the maximum value is not much higher than the average value. For some substances the maximum may be so much higher than the 24-hour average that in any real-world situation the maximum will never be reached if the 24-hour average is achieved. In such cases the 24-hour average will be limiting and the maximum will have no practical significance, except to indicate that elevated concentrations are acceptable as long as the 24-hour average is achieved.

These Guidelines have been developed on the assumption that the results of laboratory tests are generally useful for predicting what will happen in field situations. The resulting criteria are meant to apply to most bodies of water in the United States, except for the Great Salt Lake. All aquatic organisms and their common uses are meant to be considered, but not necessarily protected, if relevant data are available, with at least one specific exception. This exception is the accumulation of residues of organic compounds in the siscowet subspecies of lake trout which occurs in Lake Superior and contains up to 67% fat in the fillets (Thurston, C.E., 1962, Physical Characteristics and Chemical Composition of Two Subspecies of Lake Trout, J. Fish. Res. Bd. Canada 19:39–44). Neither siscowet nor organisms in the Great Salt Lake are intentionally protected by these Guidelines because both may be too atypical.

With appropriate modifications these Guidelines can be used to derive criteria for any specified geographical area, body of water (such as the Great Salt Lake), or group of similar bodies of water. Thus with appropriate modifications the Guidelines can be used to derive national, state, or local criteria if adequate information is available concerning the effects of the substance of concern on appropriate species and their uses. However, the basic concepts described in the Guidelines should be modified only when sound scientific evidence indicates that a criterion produced using the Guidelines would probably significantly overprotect or underprotect the presence or uses of aquatic life.

Criteria produced by these Guidelines are not enforceable numbers. They may be used in developing enforceable numbers, such as water quality standards and effluent standards. However, the development of standards may take into account additional factors such as social, legal, economic, and hydrological considerations, the environmental and analytical chemistry of the substance, the extrapolation from laboratory data to field situations, and the relationship between the species for which data are available and the species which are to be protected.

Because fresh water and salt water (including both estuarine and marine waters) have basically different chemical compositions and because freshwater and saltwater species rarely inhabit the same water simultaneously, separate criteria should be derived for these two kinds of waters. However, for some substances sufficient data may not be available to allow derivation of one or both of these criteria using the Guidelines.

These Guidelines are meant to be used after a decision is made that a criterion is needed for a substance. The Guidelines do not address the rationale for making that decision. If the potential for adverse effects on aquatic life and its uses are part of the basis for deciding whether or not a criterion is needed for a substance, these Guidelines may be helpful in the collection and interpretation of relevant data.

I. Define the Substance for Which the Criterion Is To Be Derived

A. Each separate chemical which would not ionize significantly in most natural bodies of water should usually be considered a separate substance, except possibly for structurally similar organic compounds that only differ in the number and location of atoms of a specific halogen, and only exist in large quantities as commercial mixtures of the various compounds, and apparently have similar chemical, biological, and toxicological properties.

B. For chemicals, which would ionize significantly in most natural bodies of water, such as inorganic salts, organic acids and phenols, all forms that would be in chemical equilibrium should usually be considered one substance. For metals, each different valence and each different covalently bonded organometallic compound should usually be considered a separate substance.

C. The definition of the substance may also need to take into account the analytical chemistry and fate of the substance.

II. Collect and Review Available Data

A. Collect all available data on the substance concerning (1) toxicity to, and bioaccumulation by, aquatic animals and plants, (2) FDA action levels, and (3) chronic feeding studies with wildlife.

B. Discard all data that are not available in hard copy (publication, manuscript, letter, memorandum, etc.) with enough supporting information to indicate that acceptable test procedures were used and that the results are reliable. Do not assume that all published data are acceptable.

C. Discard questionable data. For example, discard data from tests for which no control treatment existed, in which too many organisms in the control treatment died or showed signs of stress or disease, or in which distilled or deionized water was used as the dilution water for aquatic organisms. Discard data on formulated mixtures and emulsifiable concentrates of the

substance of concern, but not necessarily data on technical grade material.

D. Do not use data obtained using:

1. Brine shrimp, because they usually only occur naturally in water with salinity greater than 35 g/kg.

2. Species that do not have reproducing wild populations resident in—but not necessarily native to—North America. Resident North American species of fishes are defined as those listed in "A List of Common and Scientific Names of Fishes from the United States and Canada", 3rd ed., Special Publication No. 6, American Fisheries Society, Washington, D.C., 1970. Data obtained with non-resident species can be used to indicate relationships and possible problem areas, but cannot be used in the derivation of criteria.

3. Organisms that were previously exposed to significant concentrations of the test material or other pollutants.

III. Minimum Data Base

A. A minimum amount of data should be available to help ensure that each of the four major kinds of possible adverse effects receives some consideration. Results of acute and chronic toxicity tests with a reasonable number and variety of aquatic animals are necessary so that data available for tested species can be considered a useful indication of the sensitivities of the numerous untested species. The requirements concerning toxicity to aquatic plants are less stringent because procedures for conducting tests with plants are not as well developed and the interpretation of the results is more questionable. Data concerning bioconcentration by aquatic organisms can only be used if other relevant data are available.

B. To derive a criterion for freshwater aquatic life, the following should be available:

1. Acute tests (see Section IV) with freshwater animals in at least eight different families provided that of the eight species:
—at least one is a salmonid fish
—at least one is a non-salmonid fish
—at least one is a planktonic crustacean
—at least one is a benthic crustacean
—at least one is a benthic insect
—at least one of the benthic species is a detritivore

2. Acute-chronic ratios (see Section VI) for at least three species of aquatic animals provided that of the three species:
—at least one is a fish
—at least one is an invertebrate
—at least one is a freshwater species (the other two may be saltwater species)

3. At least one test with a freshwater alga or a chronic test with a freshwater vascular plant (see Section VIII). If plants are among the aquatic organisms that are most sensitive to the substance, tests with more than one species should be available.

4. At least one acceptable bioconcentration factor determined with an aquatic animal species, if a maximum permissible tissue concentration is available (see Section IX).

C. To derive a criterion for saltwater aquatic life, the following should be available:

1. Acute tests (see Section IV) with saltwater animals in at least eight different families provided that of the eight species:
—at least two different fish families are included
—at least five different invertebrate families are included
—either the Mysidae or Penaeidae family or both are included
—at least one of the invertebrate families is in a phylum other than Arthropoda

2. Acute-chronic ratios (see Section VI) for at least three species of aquatic animals provided that of the three species:
—at least one is a fish
—at least one is an invertebrate
—at least one is a saltwater species (the other two may be freshwater species)

3. At least one test with a saltwater alga or a chronic test with a saltwater vascular plant (see Section VIII). If plants are among the aquatic organisms most sensitive to the substance, tests with more than one species should be available.

4. At least one acceptable bioconcentration factor determined with an aquatic animal species, if a maximum permissible tissue concentration is available (see Section IX).

D. If all the requirements of the minimum data base are met, a criterion can usually be derived, except in special cases. For example, a criterion might not be possible if the acute-chronic ratios vary greatly with no apparent pattern. Also, if a criterion is to be related to a water quality characteristic, (see Sections V and VII), more data will be necessary.

Similarly, if the minimum data requirements are not satisfied, generally a criterion should not be derived, except in special cases. One such special case would be when less than the minimum amount of acute and chronic data are available, but the available data clearly indicate that the Final Residue Value would be substantially lower then either the Final Chronic Value or the Final Plant Value.

IV. Final Acute Value

A. Appropriate measures of the acute (short-term) toxicity of the substance to various species of aquatic animals are used to calculate the Final Acute Value. If acute values are available for fewer than twenty species, the Final Acute Value probably should be lower than the lowest value. On the other hand, if acute values are available for more than twenty species, the Final Acute Value probably should be higher than the lowest value, unless the most sensitive species is an important one. Although the procedure used to calculate the Final Acute Value has some limitations, it apparently is the best of the procedures currently available.

B. Acute toxicity tests should be conducted using procedures such as those described in:

ASTM Standard E 729–80, Practice for Conducting Acute Toxicity Tests with Fishes, Macroinvertebrates, and Amphibians. American Society for Testing and Materials, 1916 Race Street, Philadelphia, PA 19103.

ASTM Standard E 724–80, Practice for Conducting Static Acute Toxicity Tests with Larvae of Four Species of Bivalve Molluscs. American Society for Testing and Materials, 1916 Race Street, Philadelphia, PA 19103.

C. Results of acute tests in which food was added to the test solutions should not be used, because this may unnecessarily affect the results of the test.

D. Results of acute tests conducted with embryos should not be used (but see Section IV.E.2), because this is often an insensitive life stage.

E. Acute values should be based on endpoints and lengths of exposure appropriate to the life stage of the species tested. Therefore, only the following kinds of data on acute toxicity to aquatic animals should be used:

1. 48-hr EC50 values based on immobilization and 48-hr LC50 values for first-instar (less than 24 hours old) daphnids and other cladocerans, and second- or third-instar midge larvae.

2. 48- to 96-hr EC50 values based on incomplete shell development and 48- to 96-hr LC50 values for embryos and larvae of barnacles, bivalve molluscs (clams, mussels, oysters, and scallops), sea urchins, lobsters, crabs, shrimps, and abalones.

3. 96-hr EC50 values based on decreased shell deposition for oysters.

4. 96-hr EC50 values on immobilization or loss of equilibrium or both and 96-hr LC50 values for aquatic animals, except for cladocerans, midges, and animals whose behavior or physiology allows them to avoid

exposure to toxicant or for whom the acute adverse effect of the exposure cannot be adequately measured. Such freshwater and saltwater animals include air-breathing molluscs, unionid clams, operculate snails, and bivalve molluscs, except for some species that cannot "close up" and thus prevent exposure to toxicant, such as the bay scallop (*Argopecten irradians*).

F. For the use of LC50 or EC50 values for durations shorter and longer than those listed above, see Section X.

G. If the acute toxicity of the substance to aquatic animals has been shown to be related to a water quality characteristic such as hardness for freshwater organisms or salinity for saltwater organisms, a Final Acute Equation should be derived based on that water quality characteristic. Go to Section V.

H. If the acute toxicity of the substance has not been adequately shown to be related to a water quality characteristic, for each species for which at least one acute value is available, calculate the geometric mean of the results of all flow-through tests in which the toxicant concentrations were measured. For a species for which no such result is available, calculate the geometric mean of all available acute values, i.e., results of flow-through tests in which the toxicant concentrations were not measured and results of static and renewal tests based on initial total toxicant concentrations.

Note.—The geometric mean of N numbers is obtained by taking the N^{th} root of the product of N numbers. Alternatively, the geometric mean can be calculated by adding the logarithms of the N numbers, dividing the sum by N, and taking the antilog of the quotient. The geometric mean of two numbers can also be calculated as the square root of the product of the two numbers. The geometric mean of one number is that number. Either natural (base e) or common (base 10) logarithms can be used to calculate geometric means as long as they are used consistently within each set of data, i.e., the antilog used must match the logarithm used.

I. Count the number=N of species for which a species mean acute value is available.

J. Order the species mean acute values from low to high. Take the common logarithms of the N values (log mean values).

K. The intervals (cell widths) for the lower cumulative proportion calculations are 0.11 common log units apart, starting from the lowest log value. The value of 0.11 is an estimate of average precision and was calculated from replicate species acute values.

L. Starting with the lowest log mean value, separate the N values into intervals (or cells) calculated in Step IV. K.

M. Calculate cumulative proportions for each non-empty interval by summing the number of values in the present and all lower intervals and dividing by N. These calculations only need to be done for the first three non-empty intervals (or cells).

N. Calculate the arithmetic mean of the log mean values for each of the three intervals.

O. Using the two interval mean acute values and cumulative proportions closest to 0.05, linearly extrapolate or interpolate to the 0.05 log concentration. The Final Acute Value is the antilog of the 0.05 concentration.

In other words, where

Prop(1) and conc(1) are the cumulative proportion and mean log value for the lowest non-empty interval.

Prop(2) and conc(2) are the cumulative proportion and mean log value for the second lowest non-empty interval.

A=Slope of the cumulative proportions

B=The 0.05 log value

Then:

$A=[0.05-Prop(1)]/[Prop(2)-Prop(1)]$

$B=conc(1)+A\,[conc(2)-conc(1)]$

Final Acute Value$=10^B$

P. If for an important species, such as a recreationally or commercially important species, the geometric mean of the acute values from flow-through tests in which the toxicant concentrations were measured is lower than the Final Acute Value, then that geometric mean should be used as the Final Acute Value.

Q. Go to Section VI.

V. Final Acute Equation

A. When enough data are available to show that acute toxicity to two or more species is similarly affected by a water quality characteristic, this effect can be taken into account as described below. Pooled regression analysis should produce similar results, although data available for individual species would be weighted differently.

B. For each species for which comparable acute toxicity values are available at two or more different values of a water quality characteristic which apparently affects toxicity, perform a least squares regression of the natural logarithms of the acute toxicity values on the natural logarithms of the values of the water quality characteristic. (Natural logarithms [logarithms to the base e, denoted as ln] are used herein merely because they are easier to use on some hand calculators and computers than common logarithms [logarithms to the base 10]. Consistent use of either will produce the same result.) No transformation or a different transformation may be used if it fits the data better, but appropriate changes will be necessary throughout this section.

C. Determine whether or not each acute slope is meaningful, taking into account the range and number of values of the water quality characteristic tested. For example, a slope based on four data points may be of limited value if it is based only on data for a narrow range of values of the water quality characteristic. On the other hand, a slope based on only two data points may be meaningful if it is consistent with other information and if the two points cover a broad enough range of the water quality characteristic. If meaningful slopes are not available for at least two species or if the available slopes are not similar, return to Section IV. H., using the results of tests conducted under conditions and in water similar to those commonly used for toxicity tests with the species.

D. Calculate the mean acute slope (V) as the arithmetic average of all the meaningful acute slopes for individual species.

E. For each species calculate the geometric mean (W) of the acute toxicity values and the geometric mean (X) of the related values of the water quality characteristic.

F. For each species calculate the logarithmic intercept (Y) using the equation: $Y=\ln W-V(\ln X)$.

G. For each species calculate the species mean acute intercept as the antilog of Y.

H. Obtain the Final Acute Intercept by using the procedure described in Section IV. I–O, except insert "Intercept" for "Value".

I. If for an important species, such as a recreationally or commercially important species, the intercept calculated only from results of flow-through tests in which the toxicant concentrations were measured is lower than the Final Acute Intercept, then that intercept should be used as the Final Acute Intercept.

J. The Final Acute Equation is written as $e^{(V[\ln(\text{water quality characteristic})]+\ln Z)}$, where V=mean acute slope and Z=Final Acute Intercept.

VI. Final Chronic Value

A. The Final Chronic Value can be calculated in the same manner as the Final Acute Value or by dividing the Final Acute Value by the Final Acute-Chronic Ratio, depending on the data available. In some cases it will not be possible to calculate a Final Chronic Value.

B. Use only the results of flow-through (except renewal is acceptable for

daphnids) chronic tests in which the concentrations of toxicant in the test solutions were measured.

C. Do not use the results of any chronic test in which survival, growth, or reproduction among the controls was unacceptably low.

D. Chronic values should be based on endpoints and lengths of exposure appropriate to the species. Therefore, only the results of the following kinds of chronic toxicity tests should be used:

1. Life-cycle toxicity tests consisting of exposures of each of several groups of individuals of a species to a different concentration of the toxicant throughout a life cycle. To ensure that all life stages and life processes are exposed, the test should begin with embryos or newly hatched young less than 48 hours old (less than 24 hours old for daphnids), continue through maturation and reproduction, and with fish should end not less than 24 days (90 days for salmonids) after the hatching of the next generation. For fish, data should be obtained and analyzed on survival and growth of adults and young, maturation of males and females, embryos spawned per female, embryo viability (salmonids only) and hatchability. For daphnids, data should be obtained and analyzed on survival and young per female.

2. Partial life-cycle toxicity tests consisting of exposures of each of several groups of individuals of a species of fish to a different concentration of the toxicant through most portions of a life cycle. Partial life-cycle tests are conducted with fish species that require more than a year to reach sexual maturity, so that the test can be completed in less than 15 months, but still expose all major life stages to the toxicant. Exposure to the toxicant begins with immature juveniles at least 2 months prior to active gonad development, continues through maturation and reproduction, and ends not less than 24 days (90 days for salmonids) after the hatching of the next generation. Data should be obtained and analyzed on survival and growth of adults and young, maturation of males and females, embryos spawned per female, embryo viability (salmonids only) and hatchability.

3. Early-life-stage toxicity tests consisting of 28- to 32-days (60 days post-hatch for salmonids) exposures of the early life stages of a species of fish from shortly after fertilization through embryonic, larval, and early juvenile development. Data should be obtained and analyzed on survival and growth.

E. Do not use the results of an early-life-stage test if results of a life-cycle or partial life-cycle test with the same species are available.

F. A chronic value is obtained by calculating the geometric mean of the lower and upper chronic limits from a chronic test. A lower chronic limit is the highest tested concentration (1) in an acceptable chronic test, (2) which did not cause the occurrence (which was statistically significantly different from the control at $p=0.05$) of a specified adverse effect, and (3) below which no tested concentration caused such an occurrence. An upper chronic limit is the lowest tested concentration (1) in an acceptable chronic test, (2) which did cause the occurrence (which was statistically significantly different from the control at $p=0.05$) of a specified adverse effect and (3) above which all tested concentrations caused such an occurrence.

Note.—Various authors have used a variety of terms and definitions to interpret the results of chronic tests, so reported results should be reviewed carefully.

G. If the chronic toxicity of the substance to aquatic animals has been adequately shown to be related to a water quality characteristic such as hardness for freshwater organisms or salinity for saltwater organisms, a Final Chronic Equation should be derived based on that water quality characteristic. Go to Section VII.

H. If chronic values are available for eight species as described in Section III. B.1 or III. C.1, a species mean chronic value should be calculated for each species for which at least one chronic value is available by calculating the geometric mean of all the chronic values for the species. The Final Chronic Value should then be obtained using the procedures described in Section IV. I–O. Then go to Section VI. M.

I. For each chronic value for which at least one appropriate acute value is available, calculate an acute-chronic ratio, using for the numerator the arithmetic average of the results of all standard flow-through acute tests in which the concentrations were measured and which are from the same study as the chronic test. If such an acute test is not available, use for the numerator the results of a standard acute test performed at the same laboratory with the same species, toxicant and dilution water. If no such acute test is available, use the species mean acute value for the numerator.

Note.—If the acute toxicity or chronic toxicity or both of the substance have been adequately shown to be related to a water quality characteristic, the numerator and the denominator must be based on tests performed in the same water.

J. For each species, calcuate the species mean acute-chronic ratio as the geometric mean of all the acute-chronic ratios available for that species.

K. For some substances the species mean acute-chronic ratio seems to be the same for all species, but for other substances the ratio seems to increase as the species mean acute value increases. Thus the Final Acute-Chronic Ratio can be obtained in two ways, depending on the data available.

1. If no major trend is apparent and the acute-chronic ratios for a number of species are within a factor of ten, the final Acute-Chronic Ratio should be calculated as the geometric mean of all the species mean acute-chronic ratios available for both freshwater and saltwater species.

2. If the species mean acute-chronic ratio seems to increase as the species mean acute value increases, the value of the acute-chronic ratio for species whose acute values are close to the Final Acute Value should be chosen as the Final Acute-Chronic Ratio.

L. Calculate the Final Chronic Value by dividing the Final Acute Value by the Final Acute-Chronic Ratio.

M. If the species mean chronic value of an important species, such as a commercially or recreationally important species, is lower than the Final Chronic Value, then that species mean chronic value should be used as the Final Chronic Value.

N. Go to Section VIII.

VII. Final Chronic Equation

A. For each species for which comparable chronic toxicity values are available at two or more different values of a water quality characteristic which apparently affects chronic toxicity, perform a least squares regression of the natural logarithms of the chronic toxicity values on the natural logarithms of the water quality characteristic values. No transformation or a different transformation may be used if it fits the data better, but appropriate changes will be necessary throughout this section. It is probably preferable, but not necessary, to use the same transformation that was used with the acute values in Section V.

B. Determine whether or not each chronic slope is meaningful, taking into account the range and number of values of the water quality characteristic tested. For example, a slope based on four data points may be of limited value if it is based only on data for a narrow range of values of the water quality characteristic. On the other hand, a slope based on only two data points may be meaningful if it is consistent with other information and if the two points cover a broad enough range of the water quality characteristic. If a

meaningful chronic slope is not available for at least one species, return to Section VI. H.

C. Calculate the mean chronic slope (L) as the arithmetic average of all the meaningful chronic slopes for individual species.

D. For each species calculate the geometric mean (M) of the toxicity values and the geometric mean (P) of the related values of the water quality characteristic.

E. For each species calculate the logarithmic intercept (Q) using the equation: $Q = \ln M - L(\ln P)$.

F. For each species calculate a species mean chronic intercept as the antilog of Q.

G. Obtain the Final Chronic Intercept by using the procedure described in Section IV. I–O, except insert "Intercept" for "Value".

H. If the species mean chronic intercept of an important species, such as a commercially or recreationally important species, is lower than the Final Chronic Intercept, then that species mean chronic intercept should be used as the Final Chronic Intercept.

I. The Final Chronic Equation is written as $e^{(L[\ln(\text{Water quality characteristic})]+\ln R)}$, where L = mean chronic slope and R = Final Chronic Intercept.

VIII. Final Plant Value

A. Appropriate measures of the toxicity of the substance to aquatic plants are used to compare the relative sensitivities of aquatic plants and animals.

B. A value is a concentration which decreased growth (as measured by dry weight, chlorophyll, etc.) in a 96-hr or longer test with an alga or in a chronic test with an aquatic vascular plant.

C. Obtain the Final Plant Value by selecting the lowest plant value from a test in which the toxicant concentrations were measured.

IX. Final Residue Value

A. The Final Residue Value is derived in order to (1) prevent commercially or recreationally important aquatic organisms from exceeding relevant FDA action levels and (2) protect wildlife, including fishes and birds, that eat aquatic organisms from demonstrated adverse effects. A residue value is calculated by dividing a maximum permissible tissue concentration by an appropriate bioconcentration factor (BCF), where the BCF is the quotient of the concentration of a substance in all or part of an aquatic organism divided by the concentration in water to which the organism has been exposed. A maximum permissible tissue concentration is either (1) an action level from the FDA Administrative Guidelines Manual for fish oil or for the edible portion of fish or shellfish, or (2) a maximum acceptable dietary intake based on observations on survival, growth or reproduction in a chronic wildlife feeding study. If no maximum permissible tissue concentration is available, go to Section X because no Final Residue Value can be derived.

B. 1. A BCF determined in a laboratory test should be used only if it was calculated based on measured concentrations of the substance in the test solution and was based on an exposure that continued until either steady-state or 28-days was reached. Steady-state is reached when the BCF does not change significantly over a period of time, such as two days or 16 percent of the length of the exposure, whichever is longer. If a steady-state BCF is not available for a species, the available BCF for the longest exposure over 28 days should be used for that species.

2. A BCF from a field exposure should be used only when it is known that the concentration of the substance was reasonably constant for a long enough period of time over the range of territory inhabited by the organisms.

3. If BCF values from field exposures are consistently lower or higher than those from laboratory exposures, then only those values from field exposures should be used if possible.

4. A BCF should be calculated based on the concentration of the substance and its metabolites, which are structurally similar and are not much more soluble in water than the parent compound, in appropriate tissue and should be corrected for the concentration in the organisms at the beginning of the test.

5. A BCF value obtained from a laboratory or field exposure that caused an observable adverse effect on the test organism may be used only if it is similar to that obtained with unaffected organisms at lower concentrations in the same test.

6. Whenever a BCF is determined for a lipid-soluble substance, the percent lipids should also be determined in the tissue for which the BCF was calculated.

C. A BCF calculated using dry tissue weights must be converted to a wet tissue weight basis by multiplying the dry weight BCF value by 0.1 for plankton and by 0.2 for individual species of fishes and invertebrates.

Note.—The values of 0.2 and 0.1 were derived from data published in:

McDiffett, W. F., 1970. Ecology 51:975–988.
Brocksen, R. W., et al. 1968. J. Wildlife Management 32:52–75.
Cummins, K. W., et al. 1973. Ecology 54: 336–345.
Pesticide Analytical Manual, Volume I, Food and Drug Administration, 1969.
Love, R. M., 1957. In The Physiology of Fishes, Vol. I, M. E. Brown, ed. Academic Press, New York, p. 411.
Ruttner, F., 1963. Fundamentals of Limnology, 3rd ed. Trans. by D. G. Frey and F. E. J. Fry. Univ. of Toronto Press, Toronto.

Some additional values can be found in:

Sculthorpe, C. D., 1967. The Biology of Aquatic Vascular Plants. Arnold Publishing Ltd., London.

D. If enough pertinent data exist, several residue values can be calculated by dividing maximum permissible tissue concentrations by appropriate BCF values.

1. For each available maximum acceptable dietary intake derived from a chronic feeding study with wildlife, including birds and aquatic organisms, the appropriate BCF is based on the whole body of aquatic species which constitute or represent a major portion of the diet of the tested wildlife species.

2. For an FDA action level, the appropriate BCF is the highest geometric mean species BCF for the edible portion (muscle for decapods, muscle with or without skin for fishes, adductor muscle for scallops and total living tissue for other bivalve molluscs) of a consumed species. The highest species BCF is used because FDA action levels are applied on a species-by-species basis.

E. For lipid-soluble substances, it may be possible to calculate additional residue values. Because steady-state BCF values for a lipid-soluble chemical seem to be proportional to percent lipids from one tissue to another and from one species to another, extrapolations can be made from tested tissues or species to untested tissues or species on the basis of percent lipids.

1. For each BCF for which the percent lipids is known for the same tissue for which the BCF was measured, the BCF should be normalized to a one percent lipid basis by dividing the BCF by the percent lipids. This adjustment to a one percent lipid basis makes all the measured BCF values comparable regardless of the species or tissue for which the BCF was measured.

2. Calculate the geometric mean normalized BCF. Data for both saltwater and freshwater species can be used to determine the mean normalized BCF, because the normalized BCF seems to be about the same for both kinds of organisms.

3. Residue values can then be calculated by dividing the maximum permissible tissue concentrations by the mean normalized BCF and by a percent lipids value appropriate to the maximum permissible tissue concentration, *i.e.*,

$$\text{Residue Value} = \frac{\text{(maximum permissible tissue concentration)}}{\text{(mean normalized BCF)(appropriate percent lipids)}}$$

a. For an FDA action level for fish oil, the appropriate percent lipids value is 100.

b. For an FDA action level for fish, the appropriate percent lipids value is 15 for freshwater criteria and 16 for saltwater criteria because FDA action levels are applied on a species-by-species basis to commonly consumed species. The edible portion of the freshwater lake trout averages about 15 percent lipids, and the edible portion of the saltwater Atlantic herring averages about 16 percent lipids (Sidwell, V. D., et al. 1974 Composition of the Edible Portion of Raw (Fresh or Frozen) Crustaceans, Finfish, and Mollusks. I. Protein, Fat, Moisture, Ash, Carbohydrate, Energy Value, and Cholesterol. Marine Fisheries Review 36:21–35).

c. For a maximum acceptable dietary intake derived from a chronic feeding study with wildlife, the appropriate percent lipids is the percent lipids of an aquatic species or group of aquatic species which constitute a major portion of the diet of the wildlife species.

F. The Final Residue Value is obtained by selecting the lowest of the available residue values. It should be noted that in many cases the Final Residue Value will not be low enough. For example, a residue value calculated from an FDA action level would result in an average concentration in the edible portion of a fatty species that is at the action level. On the average half of the individuals of the species would have concentrations above the FDA action level. Also, the results of many chronic feeding studies are concentrations that cause adverse effects.

X. Other Data

Pertinent information that could not be used in earlier sections may be available concerning adverse effects on aquatic organisms and their uses. The most important of these are data on flavor impairment, reduction in survival, growth, or reproduction, or any other adverse effect that has been shown to be biologically significant. Especially important are data for species for which no other data are available. Data from behavioral, micorcosm, field, and physiological studies may also be available.

XI. Criterion

A. The criterion consists of two concentrations, one that should not be exceeded on the average in a 24-hour period and one that should not be exceeded at any time during the 24-hour period. This two-number criterion is intended to identify water quality conditions that should protect aquatic life and its uses from acute and chronic adverse effects of both cumulative and noncumulative substances without being as restrictive as a one-number criterion would have to be to provide the same degree of protection.

B. The maximum concentration is the Final Acute Value or is obtained from the Final Acute Equation.

C. The 24-hour average concentration is obtained from the Final Chronic Value, the Final Plant Value, and the Final Residue Value by selecting the lowest available value, unless other data (see Section X) from tests in which the toxicant concentrations were measured show that a lower value should be used. If toxicity is related to a water quality characteristic, the 24-hour average concentration is obtained from the Final Chronic Equation, the Final Plant Value, and the Final Residue Value by selecting the one that results in the lowest concentrations in the normal range of the water quality characteristic, unless other data (see Section X) from tests in which the toxicant concentrations were measured show that a lower value should be used.

D. The criterion is (the 24-hour average concentration) as a 24-hour average and the concentration should not exceed (the maximum concentration) at any time.

XII. Review

A. On the basis of all available pertinent laboratory and field information, determine if the criterion is consistent with sound scientific evidence. If it is not, another criterion, either higher or lower, should be derived using appropriate modifications of the Guidelines.

These Guidelines were written by Charles E. Stephan, Donald I. Mount, David J. Hansen, John H. Gentile, Gary A. Chapman and William A. Brungs of the U.S.E.P.A. Environmental Research Laboratories in Corvallis, Oregon, Duluth, Minnesota, Gulf Breeze, Florida, and Narragansett, Rhode Island. Numerous other people, many of whom do not work for U.S.E.P.A., provided assistance and suggestions.

Appendix C–Guidelines and Methodology Used in the Preparation of Health Effect Assessment Chapters of the Consent Decree Water Criteria Documents

I. Objective

The objective of the health effect assessment chapters of the ambient water criteria documents is to estimate ambient water concentrations which do not represent a significant risk to the public. These assessments should constitute a review of all relevant information on individual chemicals or chemical classes in order to derive criteria that represent, in the case of suspect or proven carcinogens, various levels of incremental cancer risk, or, in the case of other pollutants, estimates of no-effect levels.

Ideally, ambient water quality criteria should represent levels for compounds in ambient water that do not pose a hazard to the human population. However, in any realistic assessment of human health hazard, a fundamental distinction must be made between absolute safety and the recognition of some risk. Criteria for absolute safety would have to be based on detailed knowledge of dose-response relationships in humans, including all sources of chemical exposure, the types of toxic effects elicited, the existence of thresholds for the toxic effects, the significance of toxicant interactions, and the variances of sensitivities and exposure levels within the human population. In practice, such absolute criteria cannot be established because of deficiencies in both the available data and the means of interpreting this information. Consequently, the individual human health effects chapters propose criteria which minimize or specify the potential risk of adverse human effects due to substances in ambient water. Potential social or economic costs and benefits are not considered in the formulation of the criteria.

II. Types of Criteria

Ambient water quality criteria are based on three types of biological endpoints: carcinogenicity, toxicity (i.e., all adverse effects other than cancer), and organoleptic effects.

For the purpose of deriving ambient water quality criteria, carcinogenicity is regarded as a non-threshold phenomenon. Using this assumption, "safe" or "no effect" levels for carcinogens cannot be established because even extremely small doses must be assumed to elicit a finite increase in the incidence of the response. Consequently, water quality

criteria for carcinogens are presented as a range of pollutant concentrations associated with corresponding incremental risks.

For compounds which do not manifest any apparent carcinogenic effect, the threshold assumption is used in deriving a criterion. This assumption is based on the premise that a physiological reserve capacity exists within the organism which is thought to be depleted before clinical disease ensues. Alternatively, it may be assumed that the rate of damage will be insignificant over the life span of the organism. Thus, ambient water quality criteria are derived for non-carcinogenic chemicals, and presumably result in no observable-adverse-effect levels (NOAELs) in the exposed human population.

In some instances, criteria are based on organoleptic characteristics, i.e., thresholds for taste or odor. Such criteria are established when insufficient information is available on toxicologic effects or when the estimate of the level of the pollutant in ambient water based on organoleptic effects is lower than the level calculated from toxicologic data. It should be recognized that criteria based solely on organoleptic effects do not necessarily represent approximations of acceptable risk levels for human health.

Several ambient water quality criteria documents deal with classes of compounds which include chemicals exhibiting varying degrees of structural similarity. Because prediction of biological effects based solely on structural parameters is difficult, the derivation of compound-specific criteria is preferable to a class criterion. A compound-specific criterion is defined as a level derived from data on each individual subject compound that does not represent a significant risk to the public. For some chemical classes, however, a compound-specific criterion cannot be derived for each member of a class. In such instances, it is sometimes justifiable to derive a class criterion in which available data on one member of a class may be used to estimate criteria for other chemicals of the class because a sufficient data base is not available for those compounds.

For some chemicals and chemical classes, the data base was judged to be insufficient for the derivation of a criterion. In those cases, deficiencies in the available information are detailed.

III. Approach

The human health effects chapters attempt to summarize all information on the individual chemicals or classes of chemicals which might be useful in the risk assessment process to develop water quality criteria. Although primary emphasis is placed on identifying epidemiologic and toxicologic data, these assessments typically contain discussions on four topics: existing levels of human exposure, pharmacokinetics, toxic effects, and criterion formulation.

For all documents, an attempt is made to include the known relevant information. Review articles and reports are often used in the process of data evaluation and synthesis. Scientific judgment is exercised in the review and evaluation of the data in each document and in the identification of the adverse effects against which protective criteria are sought. In addition, each of these documents is reviewed by a peer committee of scientists familiar with the specific compound(s). These work groups evaluate the quality of the available data, the completeness of the data summary, and the validity of the derived criterion.

In the analysis and organization of the data, an attempt is made to be consistent with respect to the format and the application of acceptable scientific principles. Evaluation procedures used in the hazard assessment process follow the principles outlined by the National Academy of Sciences in *Drinking Water and Health* (1977) and the guidelines of the Carcinogen Assessment Group of the U.S. EPA.

A. Exposure

The exposure section of the health effects chapters reviews known information on current levels of human exposure to the individual pollutant from all sources. Much of the data was obtained from monitoring studies of air, water, food, soil, and human or animal tissue residues. The major purpose of this section is to provide background information on the contribution of water exposure relative to all other sources. Consequently, the exposure section includes subsections reviewing different routes of exposure including water and food ingestion, inhalation, and dermal contact.

Information on exposure can be valuable in developing and assessing a water quality criterion. In these documents exposure from consumption of contaminated water and contaminated fish and shellfish products is used in criterion formulation. Data for all modes of exposure are useful in relating total intake to the expected contribution from contaminated water, fish, and shellfish. In addition, information for all routes of exposure, not limited to drinking water and fish and shellfish ingestion, can be used to justify or assess the feasibility of the formulation of criteria for ambient water.

The use of fish consumption as an exposure factor requires the quantitation of pollutant residues in the edible portions of the ingested species. Accordingly, bioconcentration factors (BCFs) are used to relate pollutant residues in aquatic organisms to the pollutant concentration in the ambient waters in which they reside.

To estimate the average per capita intake of a pollutant due to consumption of contaminated fish and shellfish the results of a diet survey were analyzed to calculate the average consumption of freshwater and estuarine fish and shellfish (U.S. EPA, 1980). A species is considered to be a consumed freshwater or estuarine fish and shellfish species if at some stage in its life cycle, it is harvested from fresh or estuarine water for human consumption in significant quantities (Stephan, 1980).

Three different procedures are used to estimate the weighted average BCF depending upon the lipid solubility of the chemical and the availability of bioconcentration data.

For lipid-soluble compounds, the average BCF is calculated from the weighted average percent lipids in the edible portions of consumed freshwater and estuarine fish and shellfish which was calculated from data on consumption of each species and its corresponding percent lipids to be 3.0 percent (Stephan, 1980). Because the steady-state BCFs for lipid-soluble compounds are proportional to percent lipids, bioconcentration factors for fish and shellfish can be adjusted to the average percent lipids for aquatic organisms consumed by Americans. For many lipid-soluble pollutants, there exists at least one BCF for which the percent lipid value was measured for the tissues for which the BCF is determined.

With 3.0 percent as the weighted average percent lipids for freshwater and estuarine fish and shellfish in the average diet, a BCF, and a corresponding percent lipid value, the weighted average bioconcentration factor can be calculated.

Example:

Weighted average percent lipids for average diet = 3.0 percent

Measured BCF of 17 for trichloroethylene with bluegills at 4.8 percent lipids

Weighted average BCF for average diet equals

$$17 \times \frac{3.0\%}{4.8\%} = 10.6$$

As an estimate, 10.6 is used for the BCF.

In those cases where an appropriate bioconcentration factor is not available, the equation "Log BCF=(0.85 Log P)-0.70" can be used (Veith, et al. 1979) to estimate the BCF for aquatic organisms containing about 7.6 percent lipids (Veith, 1980) from the octanol/water partition coefficient P. An adjustment for percent lipids in the average diet versus 7.6 percent is made in order to derive the weighted average bioconcentration factor.

For non-lipid-soluble compounds, the available BCFs for the edible portion of consumed freshwater and estuarine fish and shellfish are weighted according to consumption factors to determine a weighted BCF representative of the average diet.

B. Pharmacokinetics

This section summarizes the available information on the absorption, distribution, metabolism, and elimination of the compound(s) in humans and experimental mammals. Conceptually, such information is useful in validation of inter- and intraspecies extrapolations, and in characterizing the modes of toxic action. Sufficient information on absorption and excretion in animals, together with a knowledge of ambient concentrations in water, food, and air, could be useful in estimating body burdens of chemicals in the human population. Distribution data which suggest target organs or tissues are desirable for interspecies comparison techniques. In terms of the derivation of criteria, pharmacokinetic data are essential to estimate equivalent oral doses based on data from inhalation or other routes of exposure.

C. Effects

This section summarizes information on biological effects in both humans and experimental mammals resulting in: acute, subacute, and chronic toxicity, synergism and/or antagonism, teratogenicity, mutagenicity, or carcinogenicity.

The major goal of this section is to survey the suitability of the data for use in assessment of hazard and to determine which biological end-point, i.e., non-threshold, threshold, or organoleptic, should be selected for use in criterion formulation.

Because this section attempts to assess potential human health effects, data on documented human effects are thoroughly evaluated. However, several factors inherent in human epidemiological studies usually preclude the use of such data in generating water quality criteria. These problems, as summarized by the National Academy of Sciences (NAS, 1977) are as follows:

1. Epidemiology cannot tell what effects a material will have until after humans have been exposed. One must not conduct what might be hazardous experiments on man.

2. If exposure has been ubiquitous, it may be impossible to assess the effects of a material, because there is no unexposed control group. Statistics of morbidity obtained before use of a new material can sometimes be useful, but when latent periods are variable and times of introduction and removal of materials overlap, historical data on chronic effects are usually unsatisfactory.

3. It is usually difficult to determine doses in human exposures.

4. Usually, it is hard to identify small changes in common effects, which may nonetheless be important if the population is large.

5. Interactions in a "nature-designed" experiment usually cannot be controlled.

Although these problems often prevent the use of epidemiological data in quantitative risk assessments, qualitative similarities or differences between documented effects in humans and observed effects in experimental mammals are extremely useful in testing the validity of animal-to-man extrapolations. Consequently, in each case, an attempt is made to identify and utilize both epidemiologic and animal dose-response data. Criteria derived from such a confirmed data base are considered to be reliable.

The decision to establish a criterion based on a non-threshold model is made after evaluating all available information on carcinogenicity and supportive information on mutagenicity. The approach and conditions for the qualitative decision of carcinogenicity are outlined in the U.S. EPA Interim Cancer Guidelines (41 FR 21402), in a report by Albert, et al. (1977), and in the Interagency Regulatory Liaison Group (IRLG) guidelines on carcinogenic risks (IRLG, 1979). It is assumed that a substance which induces a statistically significant carcinogenic response in animals has the capacity to cause cancer in humans. A chemical which has not induced a significant cancer response in humans or experimental animals is not identified as a carcinogen, even though its metabolites or close structural analogues might induce a carcinogenic response or it was shown to be mutagenic in an *in vitro* system.

It is recognized that some potential human carcinogens may not be identified by the guidelines given above. For example, compounds for which there is plausible but weak qualitative evidence of carcinogenicity in experimental animal systems (such as data from mouse skin painting or strain A mouse pulmonary adenoma) would be included in this category. The derivation of a criterion for human consumption from these studies in not valid, regardless of the qualitative outcome. In addition, there are certain compounds (e.g., nickel and beryllium) which were shown to be carcinogenic in humans after inhalation exposure by chemical form, but have induced thus far no response in animals or humans via ingesting their soluble salts. Nevertheless, a non-threshold criterion is developed for beryllium because tumors have been produced in animals at a site removed from the site of administration; in contrast, a threshold criterion is recommended for nickel because there is no evidence of tumors at sites distant resulting from administration of nickel solutions by either ingestion or injection.

For those compounds which were not reported to induce carcinogenic effects or for those compounds for which carcinogenic data are lacking or insufficient, an attempt is made to estimate a no-effect level. In many respects, the hazard evaluation from these studies is similar to that of bioassays for carcinogenicity. In order to more closely approximate conditions of human exposure, preference is given to chronic studies involving oral exposures in water or diet over a significant portion of the animal life span. Greatest confidence is placed in those studies which demonstrate dose-related adverse effects as well as no-effect levels.

There is considerable variability in the biological endpoints used to define a no-effect level. They may range from gross effects, such as mortality, to more subtle biochemical, physiological, or pathological changes. Teratogenicity, reproductive impairment, and behavioral effects are significant toxic consequences of environmental contamination. In instances where carcinogenic or other chronic effects occur at exposure levels below those causing teratogenicity, reproductive impairment, or behavioral effects, the former are used in deriving the criterion. For most of the compounds evaluated thus far, teratogenicity and reproductive impairment occur at doses near maximum tolerated levels with dose administration schedules well above estimated environmental exposure levels. Moreover, information on behavioral effects, which could be of

significance, is not available for most of the compounds under study. Consequently, most NOAELs derived from chronic studies are based either on gross toxic effects or on effects directly related to functional impairment or defined pathological lesions.

For compounds on which adequate chronic toxicity studies are not available, studies on acute and subacute toxicity assume greater significance. Acute toxicity studies usually involve single exposures at lethal or near lethal doses. Subacute studies often involve exposures exceeding 10 percent of the life span of the test organism, e.g., 90 days for the rat with an average life span of 30 months. Such studies are useful in establishing the nature of the compound's toxic effects and other parameters of compound toxicity, such as target organ effects, metabolic behavior, physiological/biochemical effects, and patterns of retention and tissue distribution. The utility of acute and subacute studies in deriving environmentally meaningful NOELs is uncertain, although McNamara (1976) has developed application factors for such derivations.

In some cases where adequate data are not available from studies utilizing oral routes of administration, no-effect levels for oral exposures may be estimated from dermal or inhalation studies. Such estimates involve approximations of the total dose administered based on assumptions about breathing rates and/or magnitude of absorption.

D. Criterion Rationale

This section reviews existing standards for the chemical(s), summarizes data on current levels of human exposure, attempts to identify special groups at risk, and defines the basis for the recommended criterion.

Information on existing standards is included primarily for comparison with the proposed water quality criteria. Some of the present standards, such as those recommended by the Occupational Safety and Health Administration (OSHA) or the American Conference of Governmental Industrial Hygienists (ACGIH), are based on toxicologic data but are intended as acceptable levels for occupational rather than environmental exposure. Other levels, such as those recommended by the National Academy of Sciences in *Drinking Water and Health* (1977) or in the U.S. EPA Interim Primary Drinking Water Standards, are more closely related to proposed water quality criteria. Emphasis is placed on detailing the basis for the existing standards wherever possible.

Summaries of current levels of human exposure, presented in this section, specifically address the suitability of the data to derive water quality criteria. The identification of special groups at risk, either because of geographical or occupational differences in exposure or biological differences in susceptibility to the compound(s), focuses on the impact that these groups should have on the development of water quality criteria.

The basis for the recommended criteria section summarizes and qualifies all of the data used in developing the criteria.

IV. Guidelines for Criteria Derivation

The derivation of water quality criteria from laboratory animal toxicity data is essentially a two-step procedure. First, a total daily intake for humans must be estimated which establishes either a defined level of risk for non-threshold effects or a no-effect level for threshold effects. Secondly, assumptions must be made about the contribution of contaminated water and the consumption of fish/shellfish to the total daily intake of the chemical. These estimates are then used to establish the tolerable daily intake and consequently the water quality criterion.

A. Non-Threshold Effects

After the decision has been made that a compound has the potential for causing cancers in humans and that data exist which permit the derivation of a criterion, the water concentration which is estimated to cause a lifetime carcinogenic risk of 10^{-5} is determined. The lifetime carcinogenicity risk is the probability that a person would get cancer sometime in his or her life assuming continuous exposure to the compound. The water concentration is calculated by using the low-dose extrapolation procedure proposed by Crump (1980). This procedure is an improvement on the multistage low dose extrapolation procedure by Crump, et al. (1977).

The data used for quantitative estimates are of two types: (1) lifetime animal studies, and (2) human studies where excess cancer risk has been associated with exposure to the agent. In animal studies it is assumed, unless evidence exists to the contrary, that if a carcinogenic response occurs at the dose levels used in the study, then proportionately lower responses will also occur at all lower doses, with an incidence determined by the extrapolation model discussed below.

1. Choice of Model.

There is no really solid scientific basis for any mathematical extrapolation model which relates carcinogen exposure to cancer risks at the extremely low levels of concentration that must be dealt with in evaluating the environmental hazards. For practical reasons, such low levels of risk cannot be measured directly either using animal experiments or epidemiologic studies. We must, therefore, depend on our current understanding of the mechanisms of carcinogenesis for guidance as to which risk model to use. At the present time, the dominant view of the carcinogenic process involves the concept that most agents which cause cancer also cause irreversible damage to DNA. This position is reflected by the fact that a very large proportion of agents which cause cancer are also mutagenic. There is reason to expect that the quantal type of biological response that is characteristic of mutagenesis is associated with a linear non-threshold dose-response relationship. Indeed, there is substantial evidence from mutagenesis studies with both ionizing radiation and with a wide variety of chemicals that this type of dose-response model is the appropriate one to use. This is particularly true at the lower end of the dose-response curve; at higher doses, there can be an upward curvature, probably reflecting the effects of multistage processes on the mutagenic response. The linear non-threshold dose-response relationship is also consistent with the relatively few epidemiological studies of cancer responses to specific agents that contain enough information to make the evaluation possible (e.g., radiation-induced leukemia, breast and thyroid cancer, skin cancer induced by arsenic in drinking water, and liver cancer induced by aflatoxin in the diet). There is also some evidence from animal experiments that is consistent with the linear non-threshold hypothesis (e.g., liver tumors induced in mice by 2-acetylaminofluorene in the large scale ED_{01} study at the National Center of Toxicological Research, and the initiation stage of the two-stage carcinogenesis model in the rat liver and the mouse skin).

Because it has the best, albeit limited, scientific basis of any of the current mathematical extrapolation models, the linear non-threshold model has been adopted as the primary basis for risk extrapolation to low levels of the dose-response relationship. The risk assessments made with this model should be regarded as conservative, representing the most plausible upper limit for the risk; i.e., the true risk is not likely to be higher than the estimate, but it could be smaller.

The mathematical formulation chosen to describe the linear, non-threshold dose-response relationship at low doses is the improved multistage model developed by Crump (1980). This model employs enough arbitrary constants to be able to fit almost any monotonically increasing dose-response data and it incorporates a procedure for estimating the largest possible linear slope (in the 95 percent confidence limit sense) at low extrapolated doses that is consistent with the data at all dose levels of the experiment. For this reason, it may be called a "linearized" multistage model.

2. Procedure of Low-Dose Extrapolation Based on Animal Carcinogenicity Data.

A. Description of the Extrapolation Model

Let P(d) represent the lifetime risk (probability) of cancer at dose d. The multistage model has the form

$$P(d)=1-\exp[-(q_0+q_1d+q_2d^2+\ldots+q_kd^k)]$$

where:

$q_i>0$, and $i=0, 1, 2, \ldots, k$

Equivalently,

$$A(d)=1-\exp[-(q_1d+q_2d^2+\ldots+q_kd^k)]$$

where:

$$A(d)=\frac{P(d)-P(0)}{1-P(0)},$$

is the extra risk over background rate at dose d.

The point estimate of the coefficients q_i, $i=0, 1, 2, \ldots, k$, and consequently the extra risk function A(d) at any given dose d, is calculated by maximizing the likelihood function of the data.

The point estimate and the 95 percent upper confidence limit of the extra risk A(d) are calculated by using the computer program GLOBAL 79 developed by Crump and Watson (1979). Upper 95 percent confidence limits on the extra risk and lower 95 percent confidence limits on the dose producing a given risk are determined from a 95 percent upper confidence limit, q_1^*, on parameter q_1. Whenever $q_1\neq 0$, at low doses extra risk A(d) has approximately the form $A(d)=q_1\times d$. Therefore, $q_1\times d$ is a 95 percent upper confidence limit on the extra risk and R/q_1^* is a 95 percent lower confidence limit on the dose producing an extra risk of R. Let L_0 be the maximum value of the log-likelihood function. The upper limit q_1^* is calculated buy increasing q_1 to a value q_1^* such that when the log-likelihood is again maximized subject to this fixed value q_1^* for the linear coefficient, the resulting maximum value of the log-likelihood L_1 satisfies the equation $2(L_0-L_1)=2.70554$ where 2.70554 is the cumulative 90 percent point of the chi-square distribution with one degree of freedom, which corresponds to a 95 percent upper limit (one-sided). This approach of computing the upper confidence limit for the extra risk A(d) is an improvement on the Crump, et al. (1977) model. The upper confidence limit for the extra risk calculated at low doses is always linear. This is conceptually consistent with the linear nonthreshold concept discussed earlier. The slope q_1^* is taken as an upper bound of the potency of the chemical in inducing cancer at low doses.

In fitting the dose-response model, the number of terms in the polynomial g is chosen equal to (h−1), where h is the number of dose groups in the experiment, including the control group.

Whenever the multistage model does not fit the data sufficiently, data at the highest dose is deleted and the model is refitted to the rest of the data. This is continued until an acceptable fit to the data is obtained. To determine whether or not a fit is acceptable, the chi-square statistic:

$$X^2=\sum_{i=1}^{h}\frac{(X_i-N_iP_i)^2}{N_iP_i(1-P_i)}$$

is calculated, where N_i is the number of animals in the i^{th} dose group, X_i is the number of animals in the i^{th} dose group with a tumor response, P_i is the probability of a response in the i^{th} dose group estimated by fitting the multistage model to the data, and h is the number of remaining groups.

The fit is determined to be unacceptable whenever chi-square (X^2) is larger than the cumulative 99 percent point of the chi-square distribution with f degrees of freedom, where f equals the number of dose groups minus the number of non-zero multistage coefficients.

3. Selection and Form of Data used to Estimate Parameters in the Extrapolation Model.

For some chemicals, several studies in different animal species, strains, and sexes each conducted at several doses and different routes of exposure are available. A choice must be made as to which of the data sets from several studies are to be used in the model. It is also necessary to correct for metabolism differences between species and for differences in absorption via different routes of administration. The procedures, listed below, used in evaluating these data are consistent with the estimate of a maximum-likely-risk.

a. The tumor incidence data are separated according to organ sites or tumor types. The set data (i.e., dose and tumor incidence) used in the model is set where the incidence is statistically significantly higher than the control for at least one test dose level and/or where the tumor incidence rate shows a statistically significant trend with respect to dose level. The data set which gives the highest estimate of lifetime carcinogenic risk q_1^* is selected in most cases. However, efforts are made to exclude data sets which produce spuriously high risk estimates because of a small number of animals. That is, if two sets of data show a similar dose-response relationship and one has a very small sample size, the set of data which has the larger sample size is selected for calculating the carcinogenic potency.

b. If there are two or more data sets of comparable size which are identical with respect to species, strain, sex, and tumor sites, the geometric mean of q_1^*, estimated from each of these data sets is used for risk assessment. The geometric mean of numbers $A_1, A_2, \ldots, A_m$ is defined as $(A_1\times A_2\times\ldots\times A_m)^{1/m}$

c. If sufficient data exist for two or more significant tumor sites in the same study, the number of animals with at least one of the specific tumor sites under consideration is used as incidence data in the model.

d. Following the suggestion of Mantel and Schneiderman (1975), we assume that mg/surface area/day is an equivalent dose between species. Since to a close approximation the surface area is proportional to the ⅔rds power of the weight as would be the case for a perfect sphere, the exposure in mg/⅔rds power of the body weight/day is similarly considered to be an equivalent exposure. In an animal experiment, this equivalent dose is computed in the following manner:

Let:

L_e = duration of experiment
l_e = duration of exposure
m = average dose per day in mg during administration of the agent (i.e., during l_e)
W = average weight of the experimental animal.

Then, the lifetime average exposure is

$$d=\frac{l_e\times m}{L_e\times W^{2/3}}$$

Often exposures are not given in units of mg/day, and it becomes necessary to convert the given exposures into mg/day. For example, in most feeding studies, exposure is expressed as ppm in the diet. In this case the exposure (mg/day) is derived by: $m=ppm\times F\times r$

where ppm is parts per million of the carcinogenic agent in the diet, F is the weight of the food consumed per day in kgms, and r is the absorption fraction.

In the absence of any data to the contrary, r is assumed to be one. For a uniform diet the weight of the food consumed is proportional to the calories required, which, in turn, is proportional to the surface area or the ⅔rds power of the weight, so that: $m \alpha ppm \times W^{2/3} \times r$ or

$$\frac{m}{rW^{2/3}} \alpha ppm$$

As a result, ppm in the diet is often assumed to be an equivalent exposure between species. However, we feel that this is not justified since the calories/kg of food is significantly different in the diet of man vs. laboratory animals, primarily due to moisture content differences. Instead, we use an empirically derived food factor, f=F/W, which is the fraction of a species body weight that is consumed per day as food. We use the rates given below.

Species	W	f
Man	70	0.028
Rat	0.35	0.05
Mice	0.03	0.13

Thus, when the exposure is given as a certain dietary concentration in ppm, the exposure in $mg/W^{2/3}$ is

$$\frac{m}{r \times W^{2/3}} = \frac{ppm \times F}{W^{2/3}} =$$

$$\frac{ppm \times f \times W}{W^{2/3}} = ppm \times f \times W^{1/3}$$

When exposure is given in terms of mg/kg/day=m/Wr=s the conversion is simply:

$$\frac{m}{rW^{2/3}} = s \times W^{1/3}$$

When exposure is via inhalation, the calculation of dose can be considered for two cases where (1) the carcinogenic agent is either a completely water-soluble gas or an aerosol and is absorbed proportionally to the amount of air breathed in, and (2) where the carcinogen is a poorly water-soluble gas which reaches an equilibrium between the air breathed and the body compartments. After equilibrium is reached, the rate of absorption of these agents is expected to be proportional to metabolic rate, which in turn is proportional to the rate of oxygen consumption, which in turn is a function of surface area.

Case 1

Agents that are in the form of particulate matter or virtually completely absorbed gases such as SO_2 can reasonably be expected to be absorbed proportional to the breathing rate. In this case the exposure in mg/day may be expressed as: $m=I \times v \times r$ where I is inhalation rate per day in m^3, v is mg/m^3 of the agent in air, and r is the absorption fraction.

The inhalation rates, I, for various species can be calculated from the observation (FASEB, 1974) that 25 gm mice breathe 34.5 liters/day and 113 gm rats breathe 105 liters/day. For mice and rats of other weights, W, (expressed in kg), the surface area proportionality can be used to determine breathing rates (in m^3/day) as follows:

For mice, $I=0.0345\ (W/0.025)^{2/3} m^3$/day

For rats, $I=0.105\ (W/0.113)^{2/3} m^3$/day

For humans, the values of 20 m^3/day [*] is adopted as a standard breathing rate (ICRP, 1977).

The equivalent exposure in $mg/W^{2/3}$ for these agents can be derived from the air intake data in a way analogous to the food intake data. The empirical factors for the air intake per kg per day, i=I/W based upon the previously stated relationships, are as tabulated below:

Species	W	i=I/W
Man	70	0.29
Rat	0.35	0.64
Mice	0.03	1.3

Therefore, for particulates or completely absorbed gases, the equivalent exposure in $mg/W^{2/3}$ is:

$$\frac{m}{W^{2/3}} = \frac{Ivr}{W^{2/3}} = \frac{iWvr}{W^{2/3}} = iW^{1/3} vr$$

In the absence of empirical data or a sound theoretical argument to the contrary, the fraction absorbed, r, is assumed to be the same for all species.

Case 2

The dose in mg/day of partially soluble vapors is proportional to the O_2 consumption which in turn is proportional to $W^{2/3}$ and to the solubility of gas in body fluids, which can be expressed as an absorption coefficient r for the gas. Therefore, when expressing the O_2 consumption as $O_2=k\ W^{2/3}$, where k is a constant independent of species, it follows that $m=k\ W^{2/3} \times v \times r$ or

$$d = \frac{m}{W^{2/3}} = kvr$$

As with Case 1, in the absence of experimental information or a sound theoretical argument to the contrary, the absorption fraction, r, is assumed to be the same for all species. Therefore, for these substances a certain concentration in ppm or $\mu g/m^3$ in experimental animals is equivalent to the same concentration in humans. This is supported by the observation that the minimum alveolar concentration, necessary to produce a given "stage" of anesthesia, is similar in man and animals (Dripps, et al. 1977). When the animals were exposed via the oral route and human exposure is via inhalation or vice-versa, the assumption is made, unless there is pharmacokinetic evidence to the contrary, that absorption is equal by either exposure route.

e. If the duration of experiment (L_e) is less than the natural life span of the test animal (L), the slope q_1^*, or more generally the exponent g(d), is increased by multiplying a factor $(L/L_e)^3$. We assume that if the average dose, d, is continued, the age specific rate of cancer will continue to increase as a constant function of the background rate. The age specific rates for humans increase at least by the 2nd power of the age and often by a considerably higher power, as demonstrated by Doll (1971). Thus, we would expect the cumulative tumor rate to increase by at least the 3rd power of age. Using this fact, we assume that the slope q_1^*, or more generally, the exponent g(d), would also increase by at least the 3rd power of age. As a result, if the slope q_1^* [or g(d)] is calculated at age L_e, we would expect that if the experiment had been continued for the full life span, L, at the given average exposure, the slope q_1^* [or g(d)] would have been increased by at least $(L/L_e)^3$.

This adjustment is conceptually consistent to the proportional hazard model proposed by Cox (1972) and the time-to-tumor model considered by Crump, et al. (1977) where the probability of cancer at age t and dose d is given by $P[d,t]=1-\exp[-f[t] \times g[d]]$

4. Calculation of Carcinogenic Potency Based on Human Data. If human epidemiology studies and sufficiently valid exposure information are available for the compound, they are always used in some way. If they show a carcinogenic effect, the data are analyzed to give an estimate of the linear dependence of cancer rates on lifetime average dose, which is equivalent to the factor q_1^*. If they show

[*] From "Recommendation of the International Commission on Radiological Protection," page 9, the average breathing rate is 10^7 cm^3 per 8-hour work day and 2×10^7 cm^3 in 24 hours.

no carcinogenic effect when positive animal evidence is available, then it is assumed that a risk does exist but it is smaller than could have been observed in the epidemiologic study, and an upper limit of the cancer incidence is calculated assuming hypothetically that the true incidence is just below the level of detection in the cohort studied, which is determined largely by the cohort size. Whenever possible, human data are used in perference to animal bioassay data.

In human studies, the response is measured in terms of the relative risk of the exposed cohort of individuals compared to the control group. In the analysis of this data, it is assumed that the excess risk, or relative risk minus one, $R(X)-1$, is proportional to the lifetime average exposure, X, and that it is the same for all ages. It follows that the carcinogenic potency is equal to $[R(X)-1]/X$ multiplied by the lifetime risk at that site in the general population. Except for an unusually well-documented human study, the confidence limit for the excess risk is not calculated, due to the difficulty in accounting for the uncertainty inherent in the data (exposure and cancer response).

5. Calculation of Water Quality Criteria. After the value of q_1^* in $(mg/kg/day)^{-1}$ has been determined, the lifetime risk, P, from an average daily exposure of x mg/kg/day is found from the equation $P=q_1^*x$. Therefore, if the lifetime risk is set at $P=10^{-5}$ for calculation purposes, the intake, I, in mg/day for a 70 kg person can be found by the equation: $I=70\times10^{-5}/q_1^*$ The intake of the agent from ambient water is assumed to come from two sources: (1) drinking an average of 2 liters of water per day, and (2) ingesting an average of 6.5 grams of fish per day. Because of accumulation of residues in fish, the amount of the pollutant in fish (mg/kg of edible fish) is equal to a factor R times the water concentration (mg/kg of water). Therefore, the total intake I can be written as sum of two terms: $I(mg/day)=C(mg/l)\times R(l/kg\ fish)\times 0.0065\ kg\ fish/day+C(mg/l\times 2l/day=C(2+0.0065R)$ where C is the water concentration in mg/l. Therefore, the water concentration in mg/l corresponding to a lifetime risk of 10^{-5} for a 70 kg person is calculated by the formula:

$$C = \frac{70 \times 10^{-5}}{q_1^*(2 + 0.0065\ R)}$$

B. Threshold Effects

1. Use of Animal Toxicity Data (Oral). In developing guidelines for deriving criteria based on noncarcinogenic responses, five types of response levels are considered:

NOEL—No-Observed-Effect-Level
NOAEL—No-Observed-Adverse-Effect-Level
LOEL—Lowest-Observed-Effect-Level
LOAEL—Lowest-Observed-Adverse-Effect-Level
FEL—Frank-Effect-Level

Adverse effects are defined as any effects which result in functional impairment and/or pathological lesions which may affect the performance of the whole organism, or which reduce an organism's ability to respond to an additional challenge.

One of the major problems encountered in consideration of these concepts regards the reporting of "observed effect levels" as contrasted to "observed adverse effect levels". The terms "adverse" vs. "not adverse" are at times satisfactorily defined, but due to increasingly sophisticated testing protocols, more subtle responses are being identified, resulting in a need for judgment regarding the exact definition of adversity.

The concepts listed above (NOEL, NOAEL, LOEL, LOAEL) have received much attention because they represent landmarks which help to define the threshold region in specific experiments. Thus, if a single experiment yields a NOEL, a NOAEL, a LOAEL, and a clearly defined FEL in relatively closely spaced doses, the threshold region has been relatively well defined; such data are very useful for the purpose of deriving a criterion. On the other hand, a clearly defined FEL has little utility in establishing criteria when it stands alone, because such a level gives no indication how far removed the data point is from the threshold region. Similarly, a free-standing NOEL has little utility, because there is no indication of its proximity to the LOEL, since a free-standing NOEL may be many orders of magnitude below the threshold region.

Based on the above dose-response classification system, the following guidelines for deriving criteria have been adopted:

a. A free-standing FEL is unsuitable for the derivation of criteria.

b. A free-standing NOEL is unsuitable for the derivation of criteria. If multiple NOELs are available without additional data on LOELs, NOAELs, or LOAELs, the highest NOEL should be used to derive a criterion.

c. A NOAEL, LOEL, or LOAEL can be suitable for criteria derivation. A well-defined NOAEL from a chronic (at least 90-day) study may be used directly, applying the appropriate uncertainty factor. For a LOEL, a judgment needs to be made whether it actually corresponds to a NOAEL or a LOAEL. In the case of a LOAEL, an additional uncertainty factor is applied; the magnitude of the additional uncertainty factor is judgmental and should lie in the range of 1 to 10. Caution must be exercised not to substitute "Frank-Effect-Levels" for "Lowest-Observable-Adverse-Effect-Levels".

d. If for reasonably closely spaced doses only a NOEL and a LOAEL of equal quality are available, then the appropriate uncertainty factor is applied to the NOEL.

In using this approach, the selection and justification of uncertainty factors are critical. The basic definition and guidelines for using uncertainty factors has been given by the National Academy of Sciences (1977). "Safety Factor" or "Uncertainty Factor" is defined as a number that reflects the degree or amount of uncertainty that must be considered when experimental data in animals are extrapolated to man. When the quality and quantity of experimental data are satisfactory, a low uncertainty factor is used; when data is judged to be inadequate or equivocal, a larger uncertainty factor is used. The following general guidelines have been adopted in establishing the uncertainty factors:

a. Valid experimental results from studies on prolonged ingestion by man, with no indication of carcinogenicity. Uncertainty Factor=10

b. Experimental results of studies of human ingestion not available or scanty (e.g., acute exposure only) with valid results of long-term feeding studies on experimental animals, or in the absence of human studies, valid animal studies on one or more species. No indication of carcinogenicity. Uncertainty Factor=100

c. No long-term or acute human data. Scanty results on experimental animals with no indication of carcinogenicity. Uncertainty Factor=1,000

Considerable judgment must be used in selecting the appropriate safety factors for deriving a criterion. In those cases where the data do not completely fulfill the conditions for one category and appear to be intermediate between two categories an intermediate uncertainty factor is used. Such an intermediate uncertainty factor may be developed based on a logarithmic scale (e.g., 33, being halfway between 10 and 100 on a logarithmic scale).

In determining the appropriate use of the uncertainty factors, the phrase "no

indication of carcinogenicity" is interpreted as the absence of carcinogenicity data from animal experimental studies or human epidemiology. Available short-term carcinogenicity screening tests are reported in the criteria documents, but they are not used either for derivation of numerical criteria nor to rule out the uncertainty factor approach.

Because of the high degree of judgment involved in the selection of a safety factor, the criterion derivation section of each document should provide a detailed discussion and justification for both the selection of the safety factor and the data to which it is applied. This discussion should reflect a critical review of the available data base. Factors to be considered include number of animals, species, and parameters tested; quality of controls; dose levels; route; and dosing schedules. An effort should be made to differentiate between results which constitute a toxicologically sufficient data base and data which may be spurious in nature.

2. Use of Acceptable Daily Intake (ADI). For carcinogens, the assumption of low dose linearity precludes the necessity for defining total exposure in the estimation of increased incremental risk. For non-carcinogens, ADIs and criteria derived therefrom are calculated from total exposure data that include contributions from the diet and air. The equation used to derive the criterion (C) is: $C = ADI - (DT + IN)/[2\ l + (0.0065\ kg \times R)]$ where 2 l is assumed daily water consumption, 0.0065 kg is assumed daily fish consumption, R is bioconcentration factor in units of l/kg, DT is estimated non-fish dietary intake, and IN is estimated daily intake by inhalation.

If estimates of IN and DT cannot be provided from experimental data, an assumption must be made concerning total exposure. It is recognized that either the inability to estimate DT and IN due to lack of data or the wide variability in DT and IN in different states may add an additional element of uncertainty to the criterion formulation process. In terms of scientific validity, the accurate estimate of the Acceptable Daily Intake is the major factor in satisfactory derivation of water quality criteria.

3. Use of Threshold Limit Values or Animal Inhalation Studies. Threshold Limit Values (TLVs) are established by the American Conference of Governmental and Industrial Hygienists (ACGIH) and represent 8-hour time-weighted average concentrations in air that are intended to protect workers from various adverse health effects over a normal working lifetime. Similar values are set by NIOSH (criteria) and OSHA (standards) for 10- and 8-hour exposures, respectively. To the extent that these values are based on sound toxicologic assessments and have been protective in the work environment, they provide useful information for deriving or evaluating water quality criteria. However, each TLV must be carefully examined to determine if the basis of the TLV contains data which can be used directly to derive a water quality criterion using the uncertainty factor approach. In addition, the history of each TLV must be examined to assess the extent to which it has assured worker safety. In each case, the types of effects against which TLVs are designed to protect are examined in terms of their relevance to exposure from water. It must be demonstrated that the chemical is not a localized irritant and that there is no significant effect at the site of entry irrespective of the routes of exposure (i.e., oral or inhalation).

If the TLV or similar value is recommended as the basis of the criterion, consideration of the above points is explicitly stated in the criterion derivation section of the document. Particular emphasis is placed on the quality of the TLV relative to the available toxicity data that normally is given priority over TLVs or similar established values. If the TLV can be justified as the basis for the cirterion, then the problems associated with the estimation of acceptable oral doses from inhalation data must be addressed.

Estimating equivalencies of dose-response relationships from one route of exposure to another introduces an additional element of uncertainty in the derivation of criteria. Consequently, whenever possible, ambient water quality criteria should be based on data involving oral exposures. If oral data are insufficient, data from other routes of exposure may be useful in the criterion derivation process.

Inhalation data, including TLVs or similar values, are the most common alternatives to oral data. Estimates of equivalent doses can be based upon: (1) available pharmacokinetic data for oral and inhalation routes, (2) measurements of absorption efficiency from ingested or inhaled chemicals, or (3) comparative excretion data when the associated metabolic pathways are equivalent to those following oral ingestion or inhalation. Given that sufficient pharmacokinetic data are available, the use of accepted pharmacokinetic models provides the most satisfactory approach for dose conversions. However, if available pharmacokinetic data are marginal or of questionable quality, pharmacokinetic modeling is inappropriate.

The Stokinger and Woodward (1958) approach, or similar models based on assumptions of breathing rate and absorption efficiency, represents possible alternatives when data are not sufficient to justify pharmacokinetic modeling. Such alternative approaches, however, provide less satisfactory approximations because they are not based on pharmacokinetic data. Consequently, in using the Stokinger and Woodward or related models, the uncertainties inherent in each of the assumptions and the basis of each assumption must be clearly stated in the derivation of the criterion.

The use of data pertaining to other routes of exposure to derive water quality criteria may also be considered. As with inhalation data, an attempt is made to use accepted toxicologic and pharmacokinetic principles to estimate equivalent oral doses. If simplifying assumptions are used, their bases and limitations must be clearly specified.

Because of the uncertainties involved in extrapolating from one route of exposure to another and the consequent limitations that this may place on the derived criterion, the decision to disallow such extrapolation and recommend no criterion is highly judgmental and must be made on a case-by-case basis. A decision for or against criteria derivation must balance the quantity and quality of the available data against a perceived risk to the human population.

If the Stokinger and Woodward (1958) approach is used to calculate an ADI from a TLV, the general equation is: $ADI = TLV \times BR \times DE \times d \times A_A/(A_O \times SF)$ where:

ADI = Acceptable daily intake in mg
TLV = Concentration in air in mg/m³
DE = Duration of exposure in hours per day
d = 5 days/7 days
A_A = Efficiency of absorption from air
A_O = Efficiency of absorption from oral exposure
SF = Safety factor following guidelines given above
BR = Amount of air breathed per day; assume 10 m³

For deriving an ADI from animal toxicity data, the equation is: $ADI = C_A \times D_E \times d \times A_A \times BR \times 70\ kg/(BW_A \times A_O \times SF)$ where:

ADI = Acceptable daily intake in mg
C_A = Concentration in air in mg/m³
D_E = Duration of exposure in hours per day
d = Number of days exposed/number of days observed
A_A = Efficiency of absorption from air
BR = Volume of air breathed per day in m³
70 kg = Assumed human body weight
BW_A = Body weight of experimental animals in kg

$_a$=Efficiency of absorption from oral exposure
F=Safety factor following guidelines given above.

More formal pharmacokinetic models must be developed on a compound-by-compound basis.

It should be noted that the safety factors used in the above formulae are intended to account for species variability. Consequently, the mg/surface area/day conversion factor is not used in the derivation of toxicity based criterion.

C. Organoleptic Criteria

Organoleptic criteria define concentrations of materials which impart undesirable taste and/or odor to water. In developing and utilizing such criteria two factors must be appreciated: the limitations of most organoleptic data and the human health significance of organoleptic properties.

The publications which report taste and odor thresholds are, with very few exceptions, cryptic in their descriptions of test methodologies, number of subjects tested, concentration: response relationships, and sensory characteristics at specific concentrations above threshold. Thus, the quality of organoleptic data is often significantly less than that of toxicologic data used in establishing other criteria. Consequently, a critical evaluation of the available organoleptic data must be made and the selection of the most appropriate data base for the criterion must be based on sound scientific judgment.

Organoleptic criteria are not based on toxicologic information and have no direct relationship to potential adverse human health effects. Although sufficiently intense organoleptic characteristics could result in depressed fluid intake which, in turn, might aggravate a variety of functional disease states (i.e., kidney and circulatory diseases), such effects are not used in the derivation process of organoleptic criteria unless available data would indicate an indirect human health effect via decreased fluid consumption. Criteria derived solely from organoleptic data are based upon aesthetic qualities only.

Since organoleptic and human health effects criteria are based on different endpoints, a distinction must be made between these two sets of information. In criteria summaries involving both types of data, the following format is used:

For comparison purposes, two approaches were used to derive criterion levels for ———. Based on available toxicity data, for the protection of public health the derived level is ——. Using available organoleptic data, for controlling undesirable taste and odor quality of ambient water the estimated level is ——. It should be recognized that organoleptic data as a basis for establishing a water quality criteria have no demonstrated relationship to potential adverse human health effects.

In those instances where a level to limit toxicity cannot be derived, the following statement is to be appropriately inserted:

Sufficient data are not available for ——— to derive a level which would protect against the potential toxicity of this compound.

D. Criteria for Chemical Classes

A chemical class is broadly defined as any group of chemical compounds which are reviewed in a single risk assessment document. In criterion derivation, isomers should be regarded as a part of a chemical class rather than as a single compound. A class criterion is an estimate of risk/safety which applies to more than one member of a class. It involves the use of available data on one or more chemicals of a class to derive criteria for other compounds of the same class in the event that there are insufficient data available to derive compound-specific criteria.

A class criterion usually applies to each member of a class rather than to the sum of the compounds within the class. While the potential hazards of multiple toxicant exposure are not to be minimized, a criterion, by definition, most often applies to an individual compound. Exceptions may be made for complex mixtures which are produced, released, and toxicologically tested as mixtures (e.g., toxaphene and PCBs). For such exceptions, some attempt is made to assess the effects of environmental partitioning (i.e., different patterns of environmental transport and degradation) on the validity of the criterion. If these effects cannot be assessed, an appropriate statement of uncertainty should accompany the criterion.

Since relatively minor structural changes within a class of compounds can have pronounced effects on their biological activities, reliance on class criteria should be minimized. Whenever sufficient toxicologic data are available on a chemical within a class, a compound-specific criterion should be derived. Nonetheless, for some chemical classes, scientific judgment may suggest a sufficient degree of similarity among chemicals within a class to justify a class criterion applicable to some of all members of a class.

The development of a class criterion takes into consideration the following:

1. A detailed review of the chemical and physical properties of chemicals within the group should be made. A close relationship within the class with respect to chemical acitivity would suggest a similar potential to reach common biological sites within tissues. Likewise, similar lipid solubilities would suggest the possibility of comparable absorption and tissue distribution.

2. Qualitative and quantitative data for chemicals within the group are examined. Adequate toxicologic data on a number of compounds within a group provides a more reasonable basis for extrapolation to other chemicals of the same class than minimal data on one chemical or a few chemicals within the group.

3. Similarities in the nature of the toxicologic response to chemicals in the class provides additional support for the prediction that the response to other members of the class may be similar. In contrast, where the biological response has been shown to differ markedly on a qualitative and quantitative basis for chemicals within a class, the extrapolation of a criterion to other members of that class is not appropriate.

4. Additional support for the validity of extrapolation of a criterion to other members of a class could be provided by evidence of similar metabolic and pharmacokinetic data for some members of the class.

Based on the above considerations, it may be reasonable in some cases to divide a chemical class into various subclasses. Such divisions could be based on biological endpoints (e.g., carcinogens/non-carcinogens), potency, and/or sufficiency of data (e.g., a criterion for some members of a class but no criterion for others). While no *a priori* limits can be placed on the extent of subclassification, each subclassification must be explicitly justified by the available data.

Class criteria, if properly derived and supported, can constitute valid scientific assessments of potential risk/safety. Conversely, the development of a class criterion from an insufficient data base can lead to serious errors in underestimating or overestimating risk/safety and should be rigorously avoided. Although scientific judgment has a proper role in the development of class criteria, such criteria are useful and defensible only if they are based on adequate data and scientific reasoning. The definition of sufficient data on similarities in physical, chemical, pharmacokinetic, or toxicologic properties to justify a class criterion may vary markedly depending on the degree of structural similarity and the gravity of the perceived risk. Consequently, it is imperative that the criterion derivation section of each document in which a class criterion is recommended explicity address each of the key issues discussed above, and define, as clearly as possible, the

limitations of the proposed criterion as well as the type of data needed to generate a compound-specific criterion.

A class criterion should be abandoned when there is sufficient data availabe to derive a compound-specific criterion which protects against the biological effect of primary concern; e.g., the availability of a good subchronic study would not necessarily result in the abandonment of a class criterion based on potential carcinogenicity.

The inability to derive a valid class criterion does not, and should not, preclude regulation of a compound or group of compounds based on concern for potential human health effects. The failure to recommend a criterion is simply a statement that the degree of concern cannot be quantified based on the available data and risk assessment methodology.

E. Essential Elements

Some chemicals, particularly certain metals, are essential to biological organisms at low levels but may be toxic and/ or carcinogenic at high levels. Because of potential toxic effects, it is legitimate to establish criteria for such essential elements. However, criteria must consider essentiality and cannot be established at levels which would result in deficiency of the element in the human population.

Elements are accepted as essential if listed by NAS Food and Nutrition Board or a comparably qualified panel. Elements not yet determined to be essential but for which supportive data on essentiality exists need to be further reviewed by such a panel.

To modify the toxicity and carcinogenicity based criteria, essentiality must be quantified either as a "recommended daily allowance" (RDA) or "minimum daily requirement" (MDR). These levels are then compared to estimated daily doses associated with the adverse effect of primary concern. The difference between the RDA or MDR and the daily doses causing a specified risk level for carcinogens or ADIs for non-carcinogens defines the spread of daily doses from which the criterion may be derived. Because errors are inherent in defining both essential and maximum tolerable levels, the criterion is derived from dose levels near the center of such a dose range. The decision to use either the MDR or RDA is guided by the spread of the doses and the quality of the essentiality and toxicity estimates.

The modification of criteria by consideration of essentiality must take into account all routes of exposure. If water is a significant source of the MDR or RDA, the criterion must allow for attainment of essential intake. Conversely, even when essentiality may be attained from nonwater sources, standard criteria derivation methods may be adjusted if the derived criterion represents a small fraction of the ADI or MDR. On a case-by-case basis, the modification in the use of the guidelines may include the use of different safety factors for non-carcinogens or other modifications which can be explicitly justified.

F. Use of Existing Standards

For some chemicals for which criteria are to be established, drinking water standards already exist. These standards represent not only a critical assessment of literature, but also a body of human experience since their promulgation. Therefore, it is valid to accept the existing standard unless there is compelling evidence to the contrary. This decision should be made after considering the existing standards vs. new scientific evidence which has accumulated since the standards have been established. There are several instances where the peer review process recommended usage of the present drinking water standards.

Bibliography

Albert, R.E., et al. 1977. Rationale developed by the Environmental Protection Agency for the assessment of carcinogenic risks. Jour. Natl. Can. Inst. 58: 1537.

Cox, C.R. 1972. Regression model and life tables. Jour. Roy. Stat. Soc. B. 34: 187.

Crump, K.S. 1979. Dose-response problems in carcinogenesis. Biometrics. 35: 157.

Crump, K.S. 1980. An improved procedure for low-dose carcinogenic risk assessment from animal data. Jour. Environ. Path. Toxicol. [In press].

Crump, K.S. and W.W. Watson. 1979. GLOBAL 79. A FORTRAN program to extrapolate dichotomous animal carcinogenicity data to low dose. Natl. Inst. Environ. Health Sci. Contract No. 1-ES-2123.

Crump, K.S., et al. 1977. Confidence intervals and test of hypotheses concerning dose-response relations inferred from animal carcinogenicity data. Biometrics. 33: 437.

Doll, R. 1971. Weibull distribution of cancer: Implications for models of carcinogenesis. Jour. Roy. Stat. Soc. A. 13: 133.

Dripps, R.D., et al. 1977. Introduction to Anesthesia, the Principles of Safe Practice. 5th ed. W.B. Saunders Co., Philadelphia, Pennsylvania. p. 121.

Druckrey, H. 1967. Quantitative Aspects of Chemical Carcinogenesis. *In:* R. Turhaut (ed.), Potential Carcinogenic Hazards from Drugs, Evaluation of Risks. UICC Monograph Series, Vol. 7. Springer Verlag, New York.

Federation of American Societies for Experimental Biology. 1974. Biological Data Books, 2nd ed. Vol. III. P.L. Aitman and D.S. Dittment (eds.) Federation of American Societies for Experimental Biology. Bethesda, Maryland. Library of Congress No. 72-87738.

Guess, H., et al. 1977. Uncertainty estimates for low dose rate extrapolations of animal carcinogenicity data. Can. Res. 37: 3475.

Interagency Regulatory Liaison Group. 1979. Scientific bases for identifying potential carcinogens and estimating their risks. February 6.

International Commission on Radiological Protection. 1977. Recommendation of the ICRP, Publ. No. 26, adopted January 17, 1977. Pergamon Press, Oxford, England.

Mantel, N. and M.A. Schneiderman. 1975. Estimating "safe levels," a hazardous undertaking. Can. Res. 35: 1379.

McNamara, B.P. 1976. Concepts in Health Evaluation of Commercial and Industrial Chemicals. *In:* M.A. Mehlman, et al. (eds.), Advances in Modern Toxicology, Vol. 1, Part 1. Wiley and Sons, New York. p. 61

National Academy of Sciences. 1977. Drinking Water and Health. National Academy of Sciences, Washington, D.C.

National Cancer Institute. 1976. Guidelines for carcinogen bioassay in small rodents. NCI Carcinogenesis Technical Report Series, No. 1, February, 1976.

Peto, R. 1973. Weibull distribution for continuous-carcinogenesis experiments. Biometrics. 29: 457.

Stephan, C.E. 1980. Memorandum to J. Stara. U.S. EPA. July 3.

Stokinger, M.E. and R.L. Woodward. 1958. Toxicologic methods for establishing drinking water standards. Jour. Am. Water Works Assoc. 50: 517.

U.S. EPA. 1976. National Interim Primary Drinking Water Regulations. Office of Water Supply. EPA 570/9-76-003. U.S. Environ. Prot. Agency.

U.S. EPA. 1980. Seafood consumption data analysis. Stanford Research Institute International, Menlo Park, California. Final report. Task 11, Contract No. 68-01-3887.

Veith, G.D. 1980. Memorandum to C.E. Stephan. U.S. EPA April 14.

Veith, G.D., et al. 1979. Measuring and estimating the bioconcentration factors of chemicals in fish. Jour. Fish Res. Board Can. 36: 1040.

Health Effects Methodology—Authors, Contributors and Reviewers

Jerry F. Stara, ECAO-Cin, U.S. Environmental Protection Agency
Elizabeth L. Anderson, OHEA, U.S. Environmental Protection Agency
Roy E. Albert, N.Y. University Medical School, New York, NY
Patrick R. Durkin, Syracuse Research Corporation, Syracuse, NY
Steven D. Lutkenhoff, ECAO, U.S. Environmental Protection Agency
Robert E. McGaughy, CAG, U.S. Environmental Protection Agency
Charles Ris, OHEA, U.S. Environmental Protection Agency
Lawrence Anderson, CAG, U.S. Environmental Protection Agency
Dolph Arnicar, CAG, U.S. Environmental Protection Agency
Steven Bayard, CAG, U.S. Environmental Protection Agency
Edward Calabrese, University of Massachusetts, Amherst, MA
Thomas Clarkson, University of Rochester, Rochester, NY

Joseph Cotruvo, ODW, U.S. Environmental Protection Agency
Christopher DeRosa, ECAO-Cin, U.S. Environmental Protection Agency
Kurt Enslein, Genesee Computer Center, Inc., Syracuse, NY
Jeffrey Gaba, OGC, U.S. Environmental Protection Agency
Frank Gostomski, OWRS, U.S. Environmental Protection Agency
Daniel Greathouse, HERL-Cin, U.S. Environmental Protection Agency
Joseph Arcos, Tulane University, New Orleans, LA
Dev Barnes, OWRS, U.S. Environmental Protection Agency
David L. Bayliss, CAG, U.S. Environmental Protection Agency
Chao W. Chen, CAG, U.S. Environmental Protection Agency
Herbert Cornish, University of Michigan, Ann Arbor, MI
Kenneth Crump, Science Research Systems, Inc., Ruston, LA
Michael Dourson, ECAO-Cin, U.S. Environmental Protection Agency
John R. Fowle III, CAG, U.S. Environmental Protection Agency
R. John Garner, HERL-Cin, U.S. Environmental Protection Agency
Terrence Grady, ECAO-Cin, U.S. Environmental Protection Agency
Bernard Haberman, CAG, U.S. Environmental Protection Agency
Paul Hammond, University of Cincinnati, Cincinnati, OH
Charalingayya Hiremath, CAG, U.S. Environmental Protection Agency
Dinko Kello, Institute for Medical Research and Occupational Health, Zagreb, Yugo.
Chang S. Lao, CAG, U.S. Environmental Protection Agency
Marvin Legator, University of Texas Medical Branch, Galveston, TX
Jack McGinnity, OTS, U.S. Environmental Protection Agency
Debdas Mukerjee, ECAO-Cin, U.S. Environmental Protection Agency
Ellen O'Flaherty, University of Cincinnati, Cincinnati, OH
Fred Passman, Energy Resources Co., Inc. Cambridge, MA
John F. Risher, ECAO-Cin, U.S. Environmental Protection Agency
Jeffery Rosenblatt, OTS, U.S. Environmental Protection Agency
Samuel Shibko, US FDA, Washington, DC
Harry T. Skalsky, Reynolds Metal Company
Todd W. Thorslund, CAG, U.S. Environmental Protection Agency
Benjamin VanDuuren, N.Y. University Medical School, New York, NY
James R. Withey, National Health and Welfare Canada, Ottawa, Canada
Rolf Hartung, University of Michigan, Ann Arbor, MI
Rudolf Jaeger, Harvard School of Public Health, Cambridge, MA
Arnold M. Kuzmack, CAG, U.S. Environmental Protection Agency
Si Duk Lee, ECAO-Cin, U.S. Environmental Protection Agency
Leland McCabe, HERL-Cin, U.S. Environmental Protection Agency
Myron Mehlman, Mobil Oil Corporation, New York, NY
Jean Munson, University of Cincinnati, Cincinnati, OH
Nancy Othmer, OGC, U.S. Environmental Protection Agency
David J. Reisman, ECAO-Cin, U.S. Environmental Protection Agency
Paula K. Roberson, U.S. Environmental Protection Agency
H. Daniel Roth, Roth Associates
Dharm V. Singh, CAG, U.S. Environmental Protection Agency
Robert G. Tardiff, National Academy of Sciences, Washington, DC
Anne W. Trontell, Energy Resources Co., Inc., Cambridge, MA
John Van Ryzin, Columbia University, New York, NY
Ronald E. Wyzga, Electric Power Research Institute

Appendix D—Response to Comments on Guidelines for Deriving Water Quality Criteria for the Protection of Aquatic Life and Its Uses

Introduction

Two versions of the Guidelines were published in the Federal Register for comment. The first version [43 FR 21506, May 18, 1978 and 43 FR 29028, July 5, 1979) was simply published for comment. The second [44 FR 15926, March 15, 1979) was published as part of the request for comments on the water quality criteria for 27 of the 65 pollutants. The second version was meant to be clearer and more detailed than the first, but very similar technically. Since the two versions were so similar, comments on both will be dealt with simultaneously.

Many comments were received that no draft water quality criteria for any of the 65 pollutants should have been issued for public comment until the comments on the first version of the Guidelines had been dealt with adequately and the Guidelines changed appropriately. The comments on the first version were read and the Guidelines were revised in an attempt to make the second version clearer and more detailed than the first. However, an extensive revision of the technical content of the Guidelines was not attempted between the first and second versions because the Agency was preparing water quality criteria based on the Guidelines. The Agency could have avoided this criticism simply by not publishing any version of the Guidelines for comment until March 15, 1979, but this would have greatly reduced the length of time available for people to consider the Guidelines and comment on them. As it was, some people commented that the comment period announced on March 15, 1979, was too short.

1. Comment—The procedures used to derive criteria in the "Red Book" were upheld in court and probably should still be used.

Response—The procedures used in the Guidelines are similar to some of the procedures used to develop criteria in the "Green Book", "Blue Book", and "Red Book". The Guidelines are designed to be more objective and systematic, to deal more adequately with residues, and to incorporate the concept of a minimum data base.

2. Comment—Criteria should be compilations of critically reviewed data with no synthesis or interpretation.

Response—Neither P.L. 92-500 nor the Consent Decree specify the form which a criterion must take. The Consent Decree (para. 11, p. 14) specifies that such criteria "shall state, *inter alia*, recommended maximum permissible concentrations". Adequate precedents have been set in the "Green Book", "Blue Book", and "Red Book" for the form of criteria used in the Guidelines.

3. Comment—The Guidelines and criteria should be developed by a consensus of aquatic toxicologists rather than by EPA personnel only.

Response—EPA certainly wants the Guidelines and the criteria to be as good as possible and as acceptable to as many interested people as possible. To this end, EPA has widely distributed draft versions of the Guidelines and the criteria documents, discussed them with many people, considered the comments received, and made many significant technical changes and editorial revisions. It is questionable whether or not a true consensus could have been reached by any means within the time available. In addition, EPA has a legislative responsibility which it should not delegate to someone else.

4. Comment—The Guidelines should be updated regularly.

Response—The Guidelines are not being promulgated as a regulation or directive. The purpose of presenting these Guidelines is to show how the water quality criteria for aquatic life were derived for the 65 pollutants. If EPA uses these Guidelines again, they will be revised to take into account new data, concepts, and ideas.

5. Comment—The objectives, purpose, and limitations of the Guidelines should be stated.

Response—The introductory portion of the Guidelines has been expanded to address these subjects more fully.

6. Comment—The Guidelines are too ambiguous.

Response—The Guidelines have been revised and rewritten, partly to improve clarity and provide additional details. It is not possible to provide explicit details on all items; in some areas only general guidance can be provided at this time.

EPA attempted to clearly and concisely deal with all issues which might significantly affect the resulting criteria without going into extreme detail on every potential problem. Because numerous judgments must be made, a reasonable amount of experience in aquatic toxicology will be necessary for a person to utilize the Guidelines effectively.

7. Comment—The Guidelines are too complex.

Response—Deriving a water quality criterion is a complex exercise because several different kinds of data and a wide variety of organisms need to be considered. In addition, because data have been generated using various procedures, numerous individual decisions need to be made and the Guidelines attempt to provide guidance concerning decisions that seem to need to be made frequently. The Guidelines are more complex than initially envisioned to help insure that criteria for different pollutants are derived in a reasonably comparable manner. Although the process of deriving a water quality criterion for aquatic life is complex, the Guidelines help organize the process into logical components and steps.

8. Comment—The Guidelines should be more flexible.

Response—The Guidelines are meant to provide guidance and at the same time allow reasonable flexibility. They have been used with quite a variety of pollutants for which the requirements of the minimum data base are satisfied, and they seem to be reasonably appropriate in all cases because the experiences with these substances were a major part of the basis for the Guidelines. If sound scientific evidence indicates that a particular aspect of the Guidelines is not appropriate for a specific substance, then some other more appropriate procedure should be used. However, the Guidelines should not be changed based on individual whim or personal preference.

9. Comment—The Guidelines should take into account synergism and antagonism by a wide variety of factors and the effect of the pollutant on important ecological relationships.

Response—Very little practically useful information is available on these factors in connection with the effects of pollutants on aquatic organisms. Synergism and antagonism are possible between numerous combination of two or more pollutants, and some data indicate that such interactions are not only species specific, but also vary with the ratios and absolute concentrations of the pollutants and the life stage of the species. Pollutants may affect the structure and function of aquatic ecosystems separate from their effects on individual species, but practical applications of such ideas seem very tenuous at this time. Little information is available concerning such effects, and the significance of the available data is questionable. An obviously important ecological relationship is the dependence of higher organisms on lower organisns for food. Even here, the existence of numerous lower species and their adaptability reduces the importance of any individual food species.

10. Comment—The Guidelines should take into account all identifiable effects—beneficial as well as harmful.

Response—Few tests have been conducted to identify beneficial effects of individual pollutants on aquatic organisms. However, beneficial effects are sometimes observed in chronic toxicity tests at concentrations below those that cause adverse effects. Usually in such cases the organisms in low concentrations of the pollutant are longer or heavier or reproduce more that do the controls. Even if such effects are statistically significant, they are not judged as adverse or harmful. On the other hand, a beneficial effect on one species may ultimately be to the detriment of a community if a balance between species is disturbed. Also, a concentration that benefits one species may harm a more sensitive species.

11. Comment—The Guidelines should take into account analytical methodology.

Response—The Guidelines do take into account analytical methodology in the definition of the substance, when necessary, but not in deriving the numerical value of the criterion. Concentrations which cannot be routinely measured accurately can often be measured accurately by nonroutine methods and, more importantly, do sometimes adversely affect aquatic organisms. When aquatic organisms are more sensitive than routine analytical methods, the proper solution is to develop better analytical methods, not to underprotect aquatic life. One use of criteria should be to identify needs in analytical chemistry.

12. Comment—The Guidelines should take into account (a) production and usage patterns, (b) chemical, physical and biological factors pertaining to degradation and fate of pollutants, including properties such as solubility in water, decay rate, persistence, and transformation pathways, and (c) whether or not a criterion is needed for the substance.

Response—Items included in (a) and (b) may be important in deciding whether a criterion is needed for a substance, but the Guidelines are intended to be used after the decision has been made that a criterion is needed. EPA is presently developing principles that can be used to decide whether or not a criterion is needed for a substance and items such as those listed above are probably some of the factors that should be considered when deciding whether or not a criterion is needed. If the toxicity of the chemical is used to evaluate the need for a criterion, the Guidelines may be useful in the collection and interpretation of the available toxicity data.

13. Comment—The Guidelines should take into account costs to states and industries, technological feasibility, and such characteristics of bodies of water as assimilative capacity, dispersal, dissipative factors, dilution, hydrology, mixing zones, and sediment.

Response—Factors such as these should be considered in developing standards, but not in deriving criteria. EPA is presently developing an implementation policy which will describe which of the above factors and which characteristics of the pollutant should be used, and how they should be used, in developing standards.

14. Comment—The Guidelines are not appropriate for establishing a concentration which may be present in an effluent.

Response—The Guidelines are for deriving water quality criteria, not effluent standards nor mixing zone standards nor water quality standards. Water quality criteria will probably be one factor taken into account in the development of water quality standards and toxicity-based effluent standards, but not technology-based effluent standards. EPA is presently developing policies concerning proper use of water quality criteria in various regulatory activities.

15. Comment—The derivation of criteria should be fundamentally a scientific exercise and should not employ subjective judgments.

Response—No exercise which involves the use and interpretation of data can avoid subjective judgment. Indeed, even the generation of scientific data requires subjective judgment, such as how many test organisms to use, what temperature to use, etc. One may decide to accept the recommendations of experts, but this is usually still a subjective decision. In statistics the subjective decisions are made on the basis of probability statements but the final decisions are still subjective judgments. Although the development of the Guidelines and the derivation of criteria cannot avoid subjective

decisions, gross extrapolations, wild assumptions, and novel judgments can be avoided. One can also avoid using large safety factors to "make up" for insufficient data. When some agreement exists between experts, such as on test temperature and duration of tests, the collective opinion can usually be used. EPA feels that the Guidelines do not go too far beyond the state-of-the-art and do not produce criteria by extrapolating far beyond the usefulness of the data.

16. Comment—The Guidelines should not use unproven extrapolations.

Response—EPA feels that the extrapolations used in the Guidelines are reasonable for most pollutants. Probably the most questionable extrapolation is the acute-chronic ratio, but even here an arbitrary ratio is not used. Indeed, the ratio used is usually a mean of experimentally determined acute-chronic ratios for at least three, not just one, species. In addition, the species must include at least one fish and one invertebrate. Even this amount of data does not "prove" the validity of the extrapolation, but it should provide reasonable evidence for or against the use of the ratio with any particular substance. To achieve reasonable criteria without using any extrapolations would require acute and chronic tests with many more species. This would be a high price to pay for disallowing any use of scientific inference in deriving criteria.

The early versions of the Guidelines used adjustment factors and sensitivity factors which were averages derived from data for a wide variety of substances and thus were attempts to make some extrapolations across all substances. The present version of the Guidelines is based on a minimum data base for each individual pollutant and the calculations are essentially pollutant-specific. Thus no extrapolations are made from one pollutant to another.

17. Comment—Laboratory tests overestimate the toxicity of materials because the test organisms are stressed by the artifical conditions.

Response—Laboratory conditions certainly are artificial, but they do not necessarily stress the test organisms. Organisms which survive, grow, and reproduce well in the laboratory cannot be stressed too much. Organisms in a laboratory might be considered pampered because they do not have to compete for food and are not subject to stress due to predators and changing and extreme conditions of turbidity, temperature, flow, and water quality. Also, laboratory organisms are rarely subject to stress from pollutants. Some species probably have longer average life spans in laboratories than they do in field situations.

18. Comment—Laboratory tests underestimate the toxicity of materials because the tests are usually conducted with species which are hardy, adaptable, and insensitive.

Response—Species which are readily adaptable to laboratory conditions are not necessarily insensitive as evidenced by the great range of sensitivities obtained in laboratory tests for some individual pollutants with different species. In fact, once the the proper techniques are developed, a wide variety of species can survive, grow, and reproduce well in laboratories. When the proper techniques are discovered and a species changes form "difficult" to "easy", its sensitivity does not change. Also, some species and life stages which are fragile and must be handled with great care are not particularly sensitive. On the other hand, because so few species have actually been tested in laboratories, species which are more sensitive than any of those tested in laboratories, species which are more sensitive than any of those tested probably exist for most substances.

19. Comment—Laboratory tests are artificial and contrived and do not represent the real world.

Response—Laboratory tests are indeed artificial but they are not contrived to give results that are unnecessarily high or low. Organisms in a laboratory are generally acclimated to water and conditions of constant and desirable quality, whereas in the field they are often subjected to fluctuations and extremes. Organisms in a laboratory do not have to compete for food and are not subject to predators or pollution. Organisms in the field are often exposed to more than one pollutant at a time, with the combinations and concentrations changing often.

It is true that aquatic organisms are usually exposed to instantaneous high concentrations in laboratory tests, but in field situations organisms are often not given much chance to acclimate to spills or short-term discharges. Also, some ameliorating effects occur in field, but not laboratory, situations, but such effects are not always dependable over long periods of time. The concentrations of mitigating anions, suspended solids, and complexing agents are relatively constant in some bodies of water, but not in others. Suspended solids probably do sorb and detoxify significant amounts of some pollutants, but high concentrations of suspended solids also stress some aquatic organisms. In addition, organisms are usually fed in chronic tests, so the test solution contains suspended solids and dissolved organic carbon from the food and fecal matter. Degradation and other transformations are more likely in field situations than in laboratory situations, but degradation products are not always less toxic than the undegraded material. On the other hand, many of these kinds of considerations will probably be taken into account when site-specific criteria and standards are developed under the implementation policy which is being developed by EPA.

20. Comment—Laboratory tests are poor predictors of what will happen in field situations.

Response—If conditions are comparable, laboratory toxicity tests are useful predictors of what will happen in field situations. The usefulness of such predictions will depend on how carefully one accounts for differences between species, water quality, and the form of the pollutant. Extrapolations are much more difficult for some pollutants than for others. Water quality affects the toxicity of some pollutants much more than others, and species differences, even within families, are much greater for some pollutants than for others. If such factors are taken into account, useful predictions are possible. In what is probably the most extensive comparison available of laboratory and field data (Geckler, J. R., et al. 1976. Validity of Laboratory Tests for Predicting Copper Toxicity in Streams. EPA-600/3-76-116. U.S. EPA. Duluth, MN 208 pp.), it was found that effects observed in laboratory exposures were also observed in field exposures. However, avoidance, which was not studied in laboratory exposures, was observed in the field exposures. Laboratory to field comparisons are not simple because several factors must be taken into account, the laboratory test must be conducted well and the field observations and measurements must be extensive. Although adverse effects observed in laboratory tests will usually occur in similar field situations, a problem exists with the bioaccumulation of some persistent substances. For example, PCB's seem to bioaccumulate to much higher levels in some bodies of water than they do in laboratory tests.

21. Comment—The Guidelines should place more emphasis on field information than on laboratory information.

Response—Field information on effects of pollutants on natural populations is acceptable, but the collection of definitive information of this type is high risk and costly. Few studies on the effects of pollution on natural populations provide definitive information because of the multitude of

variables that need to be taken into account. The major advantage of field studies is that conditions are natural (i.e., conditions are not controlled), but this is also the major problem with field studies. With uncontrolled conditions, numerous variables must be taken into account, because any individual variable or combination of variables may affect the results or indeed may be the cause of the results. Therefore, field studies on natural populations usually must last over several seasons and possibly over more than one year to be reasonably sure that proposed cause-and-effect relationships are real.

Another problem with field studies that are based on statistically significant differences is the power of the test. Because natural biological, spacial, and temporal variability is often rather great, a large number of samples is usually required to detect even a moderate change. A field study which purports to show that no change occurred is of no value if the power of the test calculated from the experimental design and observed variability was not high enough.

Because field studies are high cost-high risk ventures, well-designed laboratory tests are usually much more cost-effective for obtaining data on (1) the toxicity of substances to a variety of species and (2) the effect of various water quality characteristics on toxicity. Laboratory tests have been shown to generally be useful predictors of what happens in a field situation, and so it makes little sense to conduct high risk, high cost field studies rather than laboratory tests. Even definitive field studies rarely provide enough information to allow extrapolation of results to other situations, so field studies are more useful in reviewing criteria than in deriving criteria.

22. Comment—Field verification of laboratory tests and of the Guidelines are needed.

Response—Field verification of laboratory tests and of the Guidelines are certainly desirable and provide information that cannot be obtained in a laboratory. Field verification studies do not need to be as risky or as costly as studies on the effects of a pollutant on natural populations because verification studies can be designed (1) as a side-by-side comparison of the results of laboratory tests and field tests or (2) based on existing results of laboratory tests.

23. Comment—EPA should allow criteria to be derived using on-site acute toxicity tests and an application factor.

Response—This approach is usually suggested for developing effluent standards but may be just as applicable to deriving water quality criteria under certain conditions. This approach cannot be used with pollutants whose most sensitive adverse effect is due to residues. Also, it can only be used when the application factor has already been acceptably determined. Finally, acute tests must be determined with either an appropriate range of species or with an appropriate sensitive species. The implementation policy presently being developed by EPA will probably allow the use of appropriate on-site toxicity tests in the development of site-specific criteria and standards.

24. Comment—It is not clear what level of protection is intended.

Response—EPA feels that it is not possible to specify a minimum level of protection that is necessary to "protect aquatic life" or even to protect a particular species for such reasons as:

a. There are so many untested species.

b. Little practically useful information is available concerning synergism, antagonism, ecological relationships, and avoidance.

c. The effect of factors such as temperature on toxicity seems to be species-specific for at least some substances.

d. Information is not available concerning what amount of any effect would be ecologically significant and whether the amount is species-specific.

One possible conclusion is that to protect aquatic life, all species must be adequately protected. A possible extension of this would be that all criteria should be zero because any amount of any pollutant may affect some aquatic organism. Indeed, the assimilative capacity of body of water largely depends on the ability of aquatic life to "process" pollutants and to some extent, any organism which "processes" a pollutant is in some way affected by it.

The apparent level of protection is different for each kind of effect (acute toxicity to animals, chronic toxicity to animals, toxicity to plants, and bioaccumulation) because of the quality and quantity of the available information. An attempt was made to take into account such things as the importance of the effect, the quality of the available data, and the probable ecological relevance of the test methods. Thus it was felt that with regards to toxicity to animals it was probably not necessary to protect all of the species all of the time, but it certainly seems appropriate to protect most of the species most of the time and to protect important species.

On the other hand, the data base on toxicity to aquatic plants is usually very small and a variety of tests and endpoints have been used, especially with algae. Also, little information is available concerning the ecological relevance of the results of any toxicity test with algae in a concentrated test medium, especially because so many species of algae exist in each body of water.

The results of bioconcentration tests with organic chemicals, but not with inorganic chemicals, can apparently be extrapolated reasonably well based on percent lipids from one aquatic animal species to another, at least within commercially and recreationally important species. In addition, the limits on acceptable concentrations in tissue are reasonably well defined in some cases.

These kinds of considerations merely illustrate the complexity of the problem and the necessity for making decisions about each kind of effect individually. In addition, it is important to distinguish between the apparent level of protection provided by the Guidelines and the actual level of protection which will result in a field situation from the use of the implementation policy.

No attempt was made to develop Guidelines which would achieve a predetermined numerical level of protection. For each effect much desirable information is not available, and so it would be misleading to imply a level of sophistication that is not currently possible. EPA believes that the present state-of-the-art in aquatic toxicology does allow some useful conclusions about the ability of a substance to adversely affect aquatic organisms and their uses whenever the requirements of the minimum data base are satisfied, with the full realization that the resulting criterion may be somewhat overprotective or underprotective.

In almost all cases more data would be desirable and so an attempt to reach the "golden mean" will sometimes result incriteria being to high and sometimes too low. One alternative is to derive no criteria until all desirable data are available; this is unacceptable because it will almost always result in no criteria and no protection. The other alternative is to apply safety or uncertainty factors that are inversely proportional to the adequacy of the data base. In the long run this approach would encourage the generation of useful data where it was most needed, but in the short run would require many significant subjective decisions beyond the current state-of-the-art.

25. Comment—The Guidelines should not base criteria on "worst case" assumptions.

Response—The phrase "worst case assumptions" usually refers to the assumption that both the worst water quality and the most sensitive life stage occur at all times. These two assumptions are a natural result of the two concepts that criteria should be constant throughout the year and that aquatic life is not adequatley protected if it is not adequately protected throughout the year. The implementation policy being developed by EPA will determine whether site-specific criteria must be constant throughout the year. If not, then the "worst case assumptions" will not apply. Although the Guidelines might be viewed as making the "worst case assumptions", the implementation policy will determine whether the site-specific water quality criteria and standards will be based on these assumptions.

26. Comment—Safety factors should be used to protect against such things as potential subtle, but important, long term effects.

Response—Pollutants may cause many direct and indirect adverse effects which have not been studied adequately. For instance, some substances may make aquatic organisms more susceptible to disease or other stresses. In spite of such possibilities, the available information indicates that the major possible adverse effects are covered in the Guidelines and that adequate protection will usually be achieved without the use of safety factors. Safety factors would certainly offer additional protection, but the available information does not show that significant additional protection is needed.

Safety factors of from 10 to 1000 are often used to protect people mainly because people feel that people are more important than aquatic organisms and because humans are usually protected on the basis of tests with other species of animals, thus resulting in a greater uncertainty in the applicability of the results. Complete protection can only be achieved by setting all criteria at zero. Unfortunately, even "Mother Nature" sometimes seriously harms large groups of aquatic organisms, such as during droughts or severe winter freezes. EPA feels that complete protection is neither feasible, desirable, nor possible. In addition, aquatic ecosystems can recover from some adverse effects.

27. Comment—The Guidelines do not provide for an adequate margin of safety.

Response—If "margin of safety" is interpreted to mean "safety factor", then the Guidelines do not provide a margin of safety. If the Guidelines are viewed as deriving criteria for a constant quality water, then they provide a margin of safety during those portions of the year during which the most sensitive life stage does not occur. Although some species may occasionally be adversely affected, EPA feels that the Guidelines provide adequate safety because aquatic communities and their uses should not incur any substantial or permanent damage. Whether or not site-specific criteria will have a margin of safety will depend on how they are derived.

28. Comment—Criteria should be set at the least restrictive concentration and states can then apply more restrictive concentrations when necessary.

Response—It is unclear what is meant by the "least restrictive concentration" but presumably it would be a concentration which would not protect very many aquatic communities and their uses. This is contradictory to the concept that criteria are to protect aquatic life and its uses. The implementation policy being developed by EPA will allow site-specific criteria to be higher or lower than the criteria derived using the Guidelines, when adequate information is available.

29. Comment—The Guidelines should produce criteria in the form of a concentration-risk curve with appropriate confidence limits for each kind of effect.

Response—EPA feels that a risk analysis approach is certainly desirable, but far beyond the state-of-the-art at this time. When dealing with safety to humans, only one species is being protected and extrapolations are made far outside the limits of the actual test results, such as to 1 death in 100,000 people. With aquatic life, numerous species need to be protected and extrapolation far beyond the actual data is not readily accepted. In addition, safety or uncertainty factors are more readily accepted when protecting people than when protecting aquatic organisms.

Most aquatic toxicologists are not willing to let criteria for the protection of aquatic life be as dependent on mathematical models, assumptions, and manipulations as on the actual test results. Most people with experience in aquatic toxicology have an intuitive "feel" about how data should be interpreted and the Guidelines are merely an attempt to formalize a resaonable approach. The Guidelines could be written as mathematical algorithms and some approach such as error models could be developed in order to derive confidence limits. However, the algorithms and models would contain many unproven assumptions and, to be worthwhile, would undoubtedly require more data than are usually available. Although such models and algorithms would be acceptable to many statisticians and may be an appropriate future goal, the current Guidelines need to be useable by and comprehensible to current aquatic toxicologists. Most experienced aquatic toxicologists will judge the reasonableness of any set of Guidelines by comparing the resulting criteria for various pollutants with the data available for those pollutants using a "common sense" interpretation of data.

30. Comment—The Guidelines should not use unsound statistical procedures or misuse sound statistical procedures.

Response—EPA has tried to make sure that no statistical procedures are misused in the Guidelines, that no unsound statistical procedures are used, and that the purposes of the calculations are explained adequately.

31. Comment—It appears that geometric means were used instead of arithmetic means in the Guidelines to obtain lower values.

Response—Decisions such as this were made throughout the Guidelines on a case-by-case basis, and none were based on whether the resulting criteria would be higher or lower. The selection of the procedure used to calculate the mean could be based on the distribution of the values in the individual data set. Unfortunately, with small data sets rarely is it possible to reject many possible distributions and with large data sets all possible distributions are often rejected. Because many of the data sets of interest in the Guidelines are small, a reasonable approach is to base the selection of a procedure for calculating the mean on some general principles such as:

a. Sets of ratios and quotients are likely to be closer to lognormal than normal distributions. Thus geometric means, rather than arithmetic means, are used for acute-chronic ratios and for bioconcentration factors.

b. When there are numerous independent possible sources of error for each datum in a set, the error tends to be multiplicative rather than additive. Thus when the acute or chronic toxicity of a substance to a particular species is determined in different laboratories using different batches of organisms, different waters, etc, the geometric means should be used to calculate the species mean value rather than the arithmetic mean.

c. If a set of numbers approximates a lognormal distribution, the logarithms of the numbers will approximate a normal distribution.

d. The distribution of the sensitivities of individual organisms in a toxicity test

is likely to be closer to a lognormal distribution than a normal distribution. Thus the geometric mean, rather than the arithemetic mean, of the upper and lower chronic limits is used.

32. Comment—There should not be any criteria which apply to all bodies of water. Criteria should be specific for individual states, regions, other geographic areas, or bodies of water.

Response—The Guidelines are designed to provide guidance in the collection and interpretation of data concerning the effects of pollutants on aquatic life and its uses. The uses of the resulting criteria will be described by EPA in various regulations. If desired, the Guidelines can be appropriately modified and used to derive a criterion specific to one or more bodies of water or geographic areas if an appropriate data base is available. The critical literature reviews on which the criteria are based will be available for use in the derivation of local, state, or regional criteria. The latitude allowed for deriving local, state, or regional criteria and standards will be determined by the implementation policy presently being developed by EPA.

33. Comment—The Guidelines should result in criteria that are specific for individual species or groups of species (e.g., warmwater and coldwater).

Response—If the necessary data were available, criteria could be derived for any particular species or group of species. It was impractical for EPA to derive criteria for many such groups, but a relatively simple division is freshwater and saltwater organisms because these two groups rarely coexist. Most other possible general divisions of species are faced with the problem that species coexist in various combinations unless the groups are very narrow. In addition, toxicity data are rarely available for very many individual species and so data for representative species must be used, unless appropriate new data are generated. Also, the available data sometimes show wide differences within families so extrapolations from one species to another are often tenuous. Because of these problems, deriving criteria for individual species or groups of species was deemed impractical.

34. Comment—A criterion should be one number, not two.

Response—The two-number criterion is an acknowledgement that aquatic organisms can tolerate short exposures to concentrations that are higher than those they can tolerate continuously. In a two-number criterion, the higher number can assure that short-term fluctuations above the average are not too high, whereas the lower number can assure that the long-term average is not too high. A one-number criterion could be derived by using the existing 24-hour average as an instantaneous maximum. This would certainly provide additional protection, but would provide unnecessary overprotection in most cases. Because a one-number criterion would be more of an approximation than a two-number criterion, one-number criteria would be too high or too low more often and to a greater degree than two-number criteria.

35. Comment—The criteria should not specify sampling schemes.

Response—Criteria should state numerical concentration limits in terms of exposure durations because, everything else being constant, the amount of adverse effect depends on both the concentration of the pollutant and the duration of exposure. Criteria in the Green Book, Blue Book, and Red Book were usually stated as single numbers with no duration expressly stated. The implication was that the criteria were never to be exceeded at any time. Each criterion was apparently and instantaneous maximum. In practice, however, standards derived from these criteria were usually enforced on the basis of 24-hour composite samples. To avoid any ambiguity, the Guidelines specify that a criterion should be explicitly stated in terms of two time frames: an instantaneous maximum and a 24-hour average. However, this is not a specification for a sampling scheme. Standards developed from such a criterion should probably specify a sampling scheme for compliance monitoring, but it would not necessarily be in terms of point measurements and 24-hour averages.

Any sampling scheme used to determine whether or not an ambient concentration exceeds a water quality criterion or a comparable water quality standard should take into account such things as the ratio of the instantaneous maximum and the 24-hour average and the retention time of the body of water because these will primarily determine which portion of the criterion is most limiting in any specific situation. The sampling scheme should probably also take into account the cost of the analyses and results of any past analyses.

36. Comment—The criteria should be stated in terms of time frames longer that an instantaneous maximum and a 24-hour average.

Response—These two time frames were chosen because they would allow the derivation of a criterion which would be less restrictive than, but just as protective as, the previous one-number criterion. These two specific time frames were chosen because they match two kinds of samples that are commonly collected: grab samples and 24-hour composite samples. These specific time frames could probably be changed somewhat without much practical effect, but EPA saw no particular advantage to anyone to introducing novel time periods. For example, for all practical purposes in most situations a 10-minutes average is probably about the same as an instantaneous maximum.

Large increases in the time frames, however, would not provide the same amount of protection. If the instantaneous maximum were changed to a 24- or 96-hour average, and the 24-hour average were changed to a 7- or 30-day average with no change in the numerical limits, the amount of protection afforded aquatic life would fall to an unacceptable level. The longer the time span for the average, the higher the instantaneous concentration could be for short periods of time within that span. Although most chronic tests last for 28-days or longer, some chronic effects may be caused by short exposures of sensitive life stages. If the acute-chronic ratio is small, fluctuations in the instantaneous concentration may even cause acute toxicity, especially for cumulative pollutants, because for some substances the 24-, 48-, and 96-hour acute values do not differ too much.

37. Comment—A two-number criterion will be difficult to enforce.

Response—Criteria are not enforceable. Standards are enforceable. When standards to protect aquatic life are developed, they may or may not be in the same format as the criteria for aquatic life. Few standards are adequately enforced because of the high cost of continuous monitoring. The real value of many criteria and standards is in the design of waste treatment facilities; a two-number criterion should be a better basis for design than a one-number criterion.

38. Comment—The criteria should be expressed to one significant figure, not two.

Response—EPA acknowledges that there is much variability in some of the data and that the range of sensitivites is often great. When the requirements of the minimum data base are satisfied and the data agree reasonably well, two significant figures are not unreasonable. Rounding off to one significant figure could arbitrarily raise or lower the criterion by up to forty percent with no apparent consistent benefits to dischargers, regulators, or aquatic life.

39. Comment—The Guidelines should only use data for species that ought to be protected.

Response—In order to protect commercially and recreationally important species, a wide variety of "unimportant" species must also be protected. Such so-called "unimportant" species include the food organisms all the way to the bottom of the food chain. The "important" species in an aquatic community cannot maintain themselves without the help of primary producers, primary consumers, nitrifiers, dentrifiers, detritivores and saprophytes.

40. Comment—Criteria should not be based on sensitive, short-lived invertebrates.

Response—Many species of invertebrates are short-lived and are not widely distributed. However, these numerous short-lived, local species do serve important functions and should be represented in the data base. This group of organisms needs to be protected even if no one species can be considered important.

41. Comment—Criteria should protect endangered species.

Response—EPA agrees that criteria should protect endangered aquatic species. However, very few toxicity tests have been conducted with endangered species, and it does not appear feasible to require tests with such species. Endangered species are some of the many untested species which should be protected by criteria derived from available data using the Guidelines.

42. Comment—Migratory species are a special problem.

Response—Migratory species should usually be protected by criteria derived using the Guidelines unless such species are unusually sensitive. Migratory species may be especially susceptible to avoidance, but few data are available to compare species on this basis. Avoidance may be a serious latent problem because it might apply to all motile species, rather than just migratory species, and it has not been studied very much.

43. Comment—Estuarine species were ignored.

Response—The term "saltwater organisms" is meant to include estuarine species as well as true marine species.

44. Comment—The classification "invertebrates" includes species that are too dissimilar to be grouped together. These species should be separated into phyla or classes.

Response—The never-ending arguments between the "lumpers" and the "splitters" can only be resolved by considering the advantages and disadvantages of each approach in each situation. The "splitters" can usually argue that obvious differences should be taken into account and it is certainly true that shrimp are different from insects and both are different from worms. It can also be argued that there are significant differences within phyla, classes, and families. Each species could be considered a separate group, if differences between stains are arbitrarily ignored. After the species are split into separate groups, the problem then would be whether to recombine the data to derive one criterion for all species or to derive one criterion for each group. If numerous criteria are derived for a pollutant, how are these to be used to develop standards? Another problem is that unless more data are generated, the greater the number of groups, the less information there is available per group.

The basic question is "What are the important differences that need to be taken into account and how should this be done?" Because there are differences between taxonomic groups, the Guidelines require data on a number of species from a varitety of taxonomic groups. The information of each separate species is treated individually. This approach preserves the differences between species and allows all species to be considered in the development of the criterion. The number of data points is increased and the range of the data is readily apparent. Because "invertebrates" is already a large diverse group and because the range of sensitivities of fish usually overlaps that of invertebrates, little justification exists for not combining all aquatic animals.

45. Comment—Do not extrapolate from freshwater organisms to saltwater organisms or vice versa.

Response—Criteria and absolute toxicity values were not extrapolated from fresh water to salt water, but some relative data were, when it did not appear that factors such as salinity affected the data. The toxicity of some substances apparently is significantly affected by salinity, but most substances seem to have overlapping ranges of toxicity to freshwater and saltwater organisms. However, because these two kinds of organisms rarely inhabit the same body of water simultaneously, separate criteria were derived for each. Even though these two kinds of organisms are physiologically different, they do not seem to be too different toxicologically. Bioconcentration factors and acute-chronic ratios seem to be fairly similar for many freshwater and saltwater species for many pollutants, particularly organic chemicals.

46. Comment—The Guidelines base the criteria only on sensitive species and do not take into account insensitive species.

Response—The Guidelines do not necessarily base the criteria on the data for the most sensitive species. However, an aquatic ecosystem cannot be protected by protecting only the species which are insensitive. Protecting half the species will probably not protect the community. To offer reasonable protection to aquatic life and its uses, each major kind of organism and each major use must be given reasonable protection. In some cases it may in fact be necessary to protect the most sensitive species if it is a highly desirable species.

47. Comment—Species should be tested at their environmental extremes.

Response—Toxicity tests with each pollutant could indeeed be conducted with some or all species under a variety of extreme conditions and the lowest result obtained with a species could be used instead of a mean result. On the other hand, differences between results with different species seem to be much greater, and therefore more important, than the differences between results obtained with one species under different conditions. Furthermore, criteria need not necessarily protect species from all stress under the most extreme conditions, because aquatic communities and populations of individual species can recover from some perturbations.

48. Comment—Only data for species that are widely distributed, representative, critical, indigenous, important, ecologically relevant and sensitive should be used.

Response—Few species would satisfy all of the requirements that have been suggested. As more and more data are obtained with a wider variety of species for any one pollutant, it becomes more obvious that few if any species are atypically sensitive, although that may not be true for aquatic communities which contain very few species. No data exist to show that species in any one key role are toxicologically more sensitive than other kinds of species. Ecologically relevant species and species that have key roles or are relevant to the overall functioning of viable ecosystems are not necessarily toxicologically different from other species. EPA feels that if the available data cover an adequate number and variety of species, it is not necessary to try to identify and conduct tests with all important, sensitive species. In addition, the derivation of a criterion should not be based only on sensitive species, because a knowledge of the range of sensitivities may be useful. For instance, elevated concentrations of a pollutant that produces a narow range of species sensitivities are likely to cause more

damage than elevated concentrations of a pollutant that produces a wide range of species sensitivities.

49. Comment—The distinction between ionizable and unionizable compounds is not very good because some chemicals ionize and reach chemical equilibrium very slowly and others very rapidly.

Response—Most chemicals can readily be classified into one of three groups:

A. Chemicals that ionize, including hydrolyze, at least 90% and reach 90% of equilibrium in less than 8 hours in most surface waters.

B. Chemicals that ionize, including hydrolyze, less than 10% in 30 days in most surface waters.

C. Chemicals that do not fit into either one of the above categories.

For the purpose of the Guidelines, chemicals in the A group should be considered ionizable, chemicals in the B group should be considered non-ionizable, and chemicals in the C group should be classified on a case-by-case basis. Although the distinction between ionizable and unionizable may not be perfect, it is very useful for most chemicals.

50. Comment—Each individual organic compound should be considered separately.

Response—The vast majority of organic chemicals will be considered separately according to the Guidelines except for structurally similar organic compounds that meet all three specifications given in the Guidelines, such as polychlorinated biphenyls and toxaphene.

51. Comment—In-stream water quality criteria are meaningless for substances that are highly insoluble.

Response—The concentration of some substances in sediment may be important separate from the concentration of the substance in the ambient water and for these compounds a sediment quality criterion may be necessary. Generally such compounds can also cause adverse effects if the concentration in the ambient water is too high even if the concentration in the sediment is low. Thus for such compounds both kinds of criteria may be necessary rather than just one or the other.

52. Comment—If a substance is not dissolved, it is not biologically or toxicologically available.

Response—Although this may usually be true, it certainly does not apply to elemental mercury which can be oxidized and methylated to form a very toxic compound. Some organic acids and phenols and hydroxide and carbonate salts of metals have solubilities which differ substantially from one body of water to another.

53. Comment—Criteria for metals should not be for total metal.

Response—Criteria for metals will generally not be based on total metal. Most will be based on total recoverable metal because forms of metals that are not measured in the total recoverable procedure probably are not, and will not become, toxic. A major problem is that some people use a procedure for total recorverable, but report the results as total, metal. In many situations the two results are about the same, but in some cases the results are quite different.

54. Comment—The Guidelines should give more guidance for distinguishing between acceptable and unacceptable data.

Response—The Guidelines contain as much detail on this subject as EPA believes is currently feasible. Items such as the maximum acceptable control mortality and minimum number of test organisms are based on what many aquatic toxicologists generally feel are acceptable, as expressed in published methods. No data should be used in the derivation of a criteria until their quality and acceptability had been reviewed by a competent person. Competent people will occasionally disagree, but that is a fundamental property of subjective decisions.

55. Comment—Only published data should be used.

Response—Peer review is one of many concepts that is better in theory than in practice. Some poor quality data are published and some high quality data are rejected. In addition, publication is not a particularly rapid process. Whether or not data are used should depend on the applicability and quality of the data, not on whether they have been published. Data that are not published should be made readily available if they are used to derive water quality criteria.

56. Comment—All static test are unacceptable

Response—In general, high quality flow-through acute tests are preferable to high quality static acute tests, but static tests are by no means unacceptable. Few data are available to show whether static tests consistently produce acute values lower or higher or different than flow-through tests. Whereas degradation, violatilization, and buildup of metabolic products are more likely to be a problem in static tests, operator and mechanical errors are more likely in flow-through tests. Static acute tests are certainly not unacceptable for most pollutants, but static chronic tests generally are unacceptable because of changes in the toxicant concentrations and the quality of the dilution water during the test.

57. Comment—Data obtained using test organisms that were previously exposed to the pollutant should be used.

Response—Comparisons of results obtained with unexposed and previously exposed organisms should indicate whether or not acclimation has occurred. Generally, data obtained with acclimated organisms should not be used in deriving criteria because acclimated organisms are the exception rather than the norm. Rarely, if ever, can acclimation be depended on to protect organisms in a field situation because concentrations often fluctuate and motile organisms do not stay in one location very long. Data obtained with acclimated organisms may be acceptable for use in deriving some site-specific criteria.

58. Comment—Foreign species should be used to expand the data base.

Response—Foreign species may be representative of indigenous species, but some of them are quite unusual. Data obtained with foreign species may give good indications of indigenous speceis that should be used in tests on some pollutants and may identify some potential problems that should be investigated.

59. Comment—If data for brine shrimp are not used, the criteria should not apply to saline waters.

Response—Data obtained using brine shrimp are not used because these organisms are atypical. Although they may not be usually sensitive or insensitive to various pollutants, the species found in North America and used for testing only survive in the Great Salt Lake and in salt ponds near San Francisco Bay. These two habitats are unlike any others in the United States. If criteria were to be derived specifically for the Great Salt Lake or for salt ponds, then data for brine shrimp should be used.

60. Comment—Structure-activity relationships should not be used unless proven.

Response—No provision is made in the Guidelines for the use of structure-activity relationships. Such relationships may soon be well enough understood that they can be used in deriving water quality criteria.

61. Comment—A criterion should not be derived for a pollutant until data are available for a broad range of commercially, recreationally, and ecologically important species. Each species should be acutely and chronically tested under a variety of conditions in a number of different waters.

Response—Except for those people who merely want to stop EPA from deriving any water quality criteria, most people will admit that there must be some reasonable limit as to how much information is necessary concerning any regulatory action. This is as true for deriving water quality criteria, as it is for issuing NPDES permits, submitting PMNs, registering pesticides, etc. All of these regulatory activities deal with potentially significant adverse effects on aquatic organisms and should take into account many of the same possible kinds of adverse effects. Therefore, the data needs for these various activities should probably be somewhat similar, but for each regulatory activity the minimum data requirements also need to take into account the special aspects of the program and practical considerations. Unrealistic data requirements will benefit no one. It is not necessary that all questions be answered before any action is taken. It is only necessary that enough data be available to allow reasonable confidence that the water quality criteria will generally not be too high or too low.

EPA has developed minimum data requirements that describe the amounts and kinds of information that should usually be available if a criterion is to be derived using the Guidelines. When the minimum data requirements are satisfied, it should usually be possible to derive a useful criterion. The requirements take into account many things such as:

a. The existence of some species which are commerically or recreationally important and generally sensitive to some broad classes of pollutants;

b. The range of species for which data are available;

c. The cost of obtaining additional data and the usefulness of the data; and

d. The reasonableness of extrapolations from one species to another within and between groups.

The requirements set forth in the minimum data base are indeed minimal, considering the great varitey of species which exist in most aquatic ecosystems. However, EPA feels that based on the availavble information the routine requirement of more data would probably not improve criteria enough to justify the additional cost.

62. Comment—The mimimum data requirements should depend on the nature of the pollutant.

Response—EPA feels that such an approach may be feasible some time in the future, but would be an unwarrented level of sophistication at this time. For a few pollutants, it may be possible to relax some of the data requirements, but in general this can only be determined after enough data are available to indicate that a special case exists. In other cases the minimum data may indicate that additional data are highly desirable.

63. Comment—Criteria should not be derived if enough data are not available. The alternative procedures which were proposed should not be used.

Response—EPA agrees that a numerical criterion should not be derived if enough appropriate data are not available, except in some special cases. EPA also agrees that the alternative procedures which were proposed should not be used to develop numerical criteria at the present time. However, EPA feels that when a numerical criterion is not derived, a descriptive criterion can be used to accurately reflect the latest scientific knowledge.

64. Comment—The guidelines should give more guidance on relating a criterion to a water quality characteristic.

Response—More detail on this subject has been written into the Guidelines.

65. Comment—If data on the relation of toxicity and water quality are not available, no criterion should be derived.

Response—The purpose of a criterion is to present the best available information, not to ensure that all desirable information is available. Any water quality characteristic may affect the toxicity of each pollutant to some degree and it is never going to be possible to investigate all such interactions for even a few species and pollutants. EPA has adopted a minimum data base requirement for deriving a criterion, but there must be practical limits or no criterion will ever be possible. When the minimum data base requirements are satisfied, a criterion should be derived regardless of speculation that some unstudied relationship exist. When enough good data demonstrate a relation between toxicity and a water quality characteristic, an attempt should be made to use this information in the derivation of a criterion. A major purpose of site-specific criteria is to take into account the effect of local water quality conditions on toxicity.

66. Comment—Do not specify the form that a relationship between toxicity and water quality must take.

Response—The Guidelines allow the use of any set of transformations that fit the data well. The log-log model is given as an example because it seems to fit most of the available data concerning the relationship between hardness and toxicity of metals (the only such relationship for which much quantitative data are available) reasonably well.

67. Comment—The toxicity of metals should not be related to "hardness".

Response—EPA has tried to derive criteria in a form that will (a) adequately protect aquatic organisms and (b) be practically useful. Hardness is used as an easily measured surrogate for a number of interrelated water quality characteristics, such as pH, alkalinity, calcium, and magnesium. Various combinations of these probably affect individual metals differently, but these are all reasonably well correlated with hardness in a wide variety of natural waters. Some waters, such as those impacted by acid mine drainage, obviously are special cases, but they have special problems of their own.

68. Comment—Do not extrapolate slopes for toxicity vs. water quality from fish to invertebrates or from acute values to chronic values.

Response—The Guidelines do not now assume that the acute slope and the chronic slope are similar for a pollutant. On the other hand, there is no reason to believe that invertebrates are more similar than are fish and invertebrates. As explained earlier, the group "invertebrates" does not consist of a collection of species that are similar taxonomically or toxicologically. Some water quality characteristics apparently affect the toxicity of the pollutant, rather than the sensitivity of the organisms. For these kinds of factors, slopes should be the same for different species. Even factors that affect such things as the permeability of membranes may produce similar slopes for a wide variety of species. If each species must be treated separately, no criteria will ever be possible.

69. Comment—Relationships based on only two points should not be used.

Response—Two points certainly do not provide very much information about the shape, slope and position of a line. However, if other information or a reasonable assumption is available concerning the shape of the line, two good data points, spaced at a reasonable interval, can provide very useful information concerning the slope and position of the line. Three appropriately spaced points would certainly be better, and four points would be an ideal minimum.

70. Comment—Do not combine relationships that are and are not statistically significant.

Response—The Guidelines do now specify that relationships should be tested for statistical signficance. A test for statistical significance may be one indication of whether or not a slope is

useful, but such a test cannot be used with just two points and does not take into account such things as the comparability of the data, the quality of the test, and the range of the independent variable. A relationship based on six points may not be as significant as it seems if five of the points are tightly grouped.

71. Comment—The Guidelines should not combine 96-hr LC50 values and 48-hr EC50 values.

Response—Both LC50 values and EC50 values are used to measure acute toxicity of a substance to aquatic organisms. In general, an EC50 can be based on a wide variety of effects, but the Guidelines specify that the only effects to be used for deriving criteria are incomplete shell development, immobilization, and loss of equilibrium. All of these are certainly drastic effects. In a field situation these effects probably often lead to death. Just as the endpoint may be specific for the species, so may be the length of the test. The generally accepted length of an acute test with daphnids is 48 hours, whereas for most species of fish, it is 96 hours. Thus the Guidelines use both 48-hr EC50 values and 96-hr LC50 values because they are the widely accepted durations and endpoints used to measure acute toxicity to specific species.

72. Comment—Shell deposition tests are chronic tests and should not be equated with lethality tests.

Response—"Acute" implies "short" not "death". Many acute toxicity tests do use death for the effect, but many also use non-lethal effects. The shell deposition test is one of many non-lethal acute tests and is generally accepted as a short test compared to the average life span of oysters.

73. Comment—Adjustment factors should not be used to adjust for the length of the test, the technique, and unmeasured concentrations.

Response—All three kinds of adjustment factors have been deleted from the Guidelines. The factor for the length of the test was found to be unnecessary because most tests had been conducted for the standard times usually specified for the individual species. Thus the Guidelines now specify that only data from tests conducted for the time specified for the species should be used to calculate the Final Acute Value.

EPA has found that on the average flow-through acute tests give results slightly lower than do static tests, but the relationship does not seem to be too consistent and may vary from species to species for some pollutants. In addition, on the average results based on measured concerntrations do not seem to be much different from those based on unmeasured concentrations.

However, the results of flow-through tests based on measured concentrations are generally accepted as being better measures of acute toxicity than the results of flow-through tests based on unmeasured concentrations or the results of any static or renewal tests.Therefore, whenever the results of flow-through acute tests in which the concentrations were measured are available, the results of all other kinds of acute tests with that species and pollutant are not used in the calculation of the species mean acute value.

74. Comment—Species sensitivity factors should be pollutant-specific; and average factor should not be calculated for a variety of substances.

Response—EPA agrees. The requirement for acute values for at least eight different species was developed in part to allow for a reasonably good calculation of a mean acute value and a species sensitivity factor for each individual pollutant. A better way of using the acute values for the individual species has been developed, but no extrapolations are made from one pollutant to another.

75. Comment—The distribution of species mean acute values for a pollutant will be truncated if the species cannot be killed or affected by concentrations above solubility.

Response—Some species are so resistant to some pollutants that they cannot be killed or affected in acute tests even by concentrations which are much above solubility. Such "greater than" values cannot be used in the calculation of means and variances for pollutants. When the "greater than" values are for insensitive species and are at or above solubility, the values can be used in the calculation of the Final Acute Value by adjusting the cumulative proportions for all the speices with quantitative values. The shape of the curve at the high end cannot be determined, but the Final Acute Value is more dependent on the species mean acute values and the cumulative probabilities at the low end.

76. Comment—Early life-stage tests with fish should be used interchangeably with life-cycle and partial life-cycle tests with fish.

Response—EPA agrees that early life-stage tests with fish generally give about the same results as comparable life-cycle and partial life-cycle tests. However, because the shorter test is merely a predictor of the longer tests, whenever both kinds of results are available, the results of life-cycle and partial life-cycle tests should be used instead of the results of early life-stage tests.

77. Comment—Appropriate measures of chronic toxicity and appropriate lengths of exposure should be defined.

Response—The descriptions of appropriate chronic tests have been clarified.

78. Comment—The factor of 0.44 should not be used.

Response—It is not now used.

79. Comment—The Final Chronic Value should not be lower than the lowest measured species chronic value, even if chronic data are not available for sensitive species.

Response—Aquatic ecosystems cannot be protected from chronic toxicity by protecting only the insensitive species from chronic toxicity. In the past both arbitrary and experimentally determined application factors have been used to relate acute and chronic toxicity. For a variety of reasons the Guidelines do not use an application factor, but instead use the acute-chronic ratio, which is similar to the inverse of an application factor. Thus the acute-chronic ratio should normally be greater than one. The acute-chronic ratio is to be used with invertebrates as well as fish and is to be an experimentally determined value for each individual pollutant. The acute-chronic ratio should also avoid the confusion as to whether a large application factor is one that is close to unity or one that has a denominator that is much larger than the numerator. The acute-chronic ratio is calculated by dividing the appropriate measure of acute toxicity for the species (as specified in the Guidelines) by the appropriate measure of chronic toxicity for the same species (as specified in the Guidelines).

Some people have confused application factors and safety factors and use of the term "acute-chronic ratio" should help avoid this problem. Acute-chronic ratios are a way of estimating the chronic sensitivity of a species for which no chronic toxicity data are available. Safety factors would provide an extra margin of safety beyond the sensitivity of the species. Safety or uncertainty factors are intended to reduce the possibility of underprotection, whereas acute-chronic ratios are intended to estimate the actual chronic sensitivity of the species to the pollutant. This estimate is just as likely to be too high as it is to be too low. A mean acute-chronic ratio will in fact be too high for half the species and too low for the other half.

When three or more acute-chronic ratios have been determined for a pollutant with both fish and

nvertebrates, three patterns have been bserved when the individual species re listed in order of their species mean cute values:

a. The ratios randomly differ by a actor of ten or more.

b. The ratio appears to be about the ame (within a factor of ten) for all pecies.

c. Species with higher acute values lso have higher acute-chronic ratios.

The available data indicate that fish nd invertebrates do not consistently ave different acute-chronic ratios and hat for some pollutants freshwater and altwater species have similar acute-hronic ratios.

80. Comment—No application factor hould be used unless it is specific for he pollutant, species, and water.

Response—There is no point in using n application factor or acute-chronic atio or any concept if it does not allow ome generalization or extrapolation rom one species to another or from one vater to another. Not allowing any eneralizations or extrapolations would equire that much data be generated for ach species and each pollutant in each vater in which a criterion is necessary. When enough supporting data are vailable, extrapolations using such hings as acute-chronic ratios are cost-ffective and scientifically sound.

81. Comment—Additional levelopment of methodology for toxicity ests with aquatic plants is needed.

Response—This is most certainly true. Much other research also is needed, and enerally is considered higher priority. EPA hopes that someday all of the dditional research that needs to be lone will be done. Few pollutants seem o affect aquatic plants at oncentrations which do not chronically ffect aquatic animals, and it is hoped hat this is not an artifact of the test nethods currently used.

82. Comment—Data on toxicity to lants should not be used for deriving riteria because plants are more site-pecific than animals.

Response—Numerous species of lants, especially algae, exist in most odies of water. On the other hand, EPA nows of no data to support the ontention that the sensitivities of quatic plants are any more site-specific han those of aquatic animals, or that he range of sensitivities between plants s as great as that for animals. One pecies may or may not be epresentative of other species. After the nethodology for toxicity tests with quatic plants is better developed, tests vith a wider variety of species would ertainly be desirable.

83. Comment—The Final Plant Value hould not be the lowest available plant value based on measured concentrations.

Response—EPA adopted the procedure described in the Guidelines for obtaining the Final Plant Value for several reasons including:

a. The methodology for toxicity tests with aquatic plants is not well developed.

b. For only a few pollutants have toxicity tests been conducted with more than a very few species of plants.

c. Little is known about the range of sensitivities of various species of aquatic plants.

d. Based on available data, almost no pollutants are toxic to aquatic plants at the lowest concentrations which are chronically toxic to aquatic animals or cause unacceptable residues.

84. Comment—Residue accumulation in any part of an aquatic ecosystem should be prevented as much as possible.

Response—Accumulation of residues in aquatic organisms only becomes a problem if the concentration of residue is high enough to adversely affect either (a) the organism itself, (b) a consumer of the organism, or (c) the marketability of the organism. Adverse effects on the aquatic organism itself will be detected in acute and chronic toxicity tests. The use of FDA action levels and chronic feeding studies with wildlife are designed to protect the uses and consumers of aquatic organisms.

85. Comment—Bioconcentration factors (BCFs) derived from field data should not be used.

Response—EPA feels that BCFs derived from adequate data, whether they be laboratory data or field data, should be used. More data are necessary to document a BCF from a field exposure than a laboratory exposure, as specified in the Guidelines, but if enough data are available, field BCFs should be used.

86. Comment—Kinetically derived bioconcentration factors (BCFs) should be used.

Response—Kinetically derived BCFs should be used if the bioconcentration test lasted long enough, *i.e.*, to apparent steady-state, to verify that the model (assumptions) used in the calculations actually fits the data for the individual pollutant.

87. Comment—Bioconcentration factors (BCFs) should not be estimated from octanol-water partition coefficients.

Response—The available data seem to indicate a reasonably good relationship for lipid-soluble substances between steady-state BCFs and octanol-water partition coefficients. BCFs estimated from partition coefficients are not used in the Guidelines because measured BCFs are available for all pollutants for which a maximum permissible tissue concentration is available.

88. Comment—Bioconcentration factors (BCFs) are dependent on temperature, food, salinity, stress, and other things.

Response—Many things such as these probably do affect BCFs. Until data are available to show that such effects are important and are not species-specific, little needs to be, or can be, done to take such factors into account when deriving water quality criteria.

89. Comment—Bioconcentration factors (BCFs) should be based only on tissues that are actually eaten.

Response—Although people usually only eat muscle tissue of fish, wildlife usually eat the whole body of fish. The tissues used in the determination of BCFs must be appropriate to the kind of consumer organism or regulatory action. On the other hand, since the BCF for a lipid-soluble substance seems to be proportional to percent lipids, extrapolations can be made on the basis of percent lipids regardless of the tissue.

90. Comment—Chronic toxicity tests with rats and mice should not be used as representative of tests on mammalian wildlife.

Response—Because results of tests on a variety of species are extrapolated to man, it should be just as reasonable to extrapolate from one mammalian species to another mammalian species within certain limits. However, such extrapolations are not now used in the Guidelines; only the results of chronic toxicity tests with wildlife are used to protect wildlife consumers of aquatic life.

91. Comment—Information concerning bioconcentration should only be used if such information is used to protect aquatic organisms, not to protect the marketability of aquatic organisms.

Response—Protection of aquatic organisms must include not only the protection of the existence of aquatic organisms, but also protection of the common uses of aquatic organisms. Commercially important aquatic organisms cannot be considered adequately protected if they cannot be sold. The Guidelines do not use any data pertaining to safety to humans in an attempt to protect human consumers of aquatic organisms. Instead, the Guidelines merely attempt to ensure that residues in aquatic organisms do not exceed FDA action levels so that the uses of commercially and recreationally important species are not restricted by the Food and Drug Administration.

92. Comment—A Final Residue Value calculated from an FDA action level is actually a concentration that will result in the average concentration in some species being at the FDA action level.

Response—This is a good point. A similar situation exists when the calculation is based on a concentration which caused an adverse effect in a chronic wildlife feeding study. In all such cases, the Final Residue Value should be lower, but EPA knows of no non-arbitrary way to determine how much lower the value should be.

93. Comment—The FDA action levels for finished animal feed should not be used.

Response—They are not now used.

94. Comment—Flavor impairment should not be used to derive water quality criteria for aquatic life.

Response—Many of the commercially and recreationally important aquatic orgnaisms are consumted by people. If the flavor is significantly impaired, the use of these species will be adversely affected. Flavor impairment should be considered an effect that can adversely affect the use of aquatic organisms.

95. Comment—The instructions for using the other data are not very detailed and are not mathematical.

Response—EPA has tried to include as much detail in the instructions for using the other data as are currently justified. Extensive detail and mathematical treatment are not deemed realistic at this time because so little information is available concerning the various kinds of other data.

96. Comment—The final review of the criteria should allow revision up or down based on sound scientific evidence.

Response—The Guidelines always have allowed revision up or down, but this is now stated explicitly in the Guidelines.

97. Comment—Some bodies of water, such as some USGS benchmark streams and the Houston ship channel, contain concentrations above the criteria for some pollutants and still contain aquatic communities that are diverse, healthy, and productive. Such information should be used in the review of the criteria because it indicates that some criteria are too low.

Response—Rarely are there enough data available to accurately identify the concentrations of pollutants to which aquatic organisms in bodies of water are actually exposed. The sampling scheme should provide a good estimate of the mean and variance of the concentration: a few grab or composite samples cannot provide enough information to characterize the concentrations of pollutants in most bodies of water. The concentrations vary not only with time but also with location at each time, so the samples must be taken where the organisms of interest are located at that time.

A more serious problem concerns the definition of an acceptable aquatic ecosystem. How does one determine if an aquatic ecosystem is healthy or productive? If a diverse system is, by definition, healthy, is it also, by definition, productive? What is the minimum acceptable diversity? What is the minimum acceptable productivity? Should the acceptable levels of diversity and productivity be site-specific? Is a body of water acceptable just because no dead fish are observed. How many pounds of trout should a trout stream produce each year to be considered healthy and productive? How does one treat motile species that may avoid some periodic increases in pollution levels? Is an aquatic ecosystem healthy and productive if the normally edible portion of a consumed species tastes bad or contains excessive residues? Questions such as these indicate the difficulty of quantitatively judging the quality of aquatic ecosystems on the basis of their acceptability or usefulness to man or on any other basis. Although judging bodies of water would be a difficult job, it certainly could be done by a competent group of trained professionals. The point is that it is not as easy a job as some people would like to think. There are also people who feel that various pristine bodies of water should be managed because they are not as productive as they could be.

As mentioned earlier, the criteria documents derive criteria which may be too high or too low for some specific bodies of water. With appropriate modifications the Guidelines can be used to derive criteria for any specific body of water or geographic area. In addition, it is certainly possible that one or more factors which affect the toxicity of one or more pollutants may not have been studied very throughly or even identified yet. The criteria are based on the best available information and the state-of-the-art of aquatic toxicology, but it is always possible that something important has not been adequately studied by regulators, discharges or academia.

Appendix E.—Responses to Public Comments on the Human Health Effects Methodology for Deriving Ambient Water Quality Criteria

I. Introduction

On March 15, 1979, the U.S. Environmental Protection Agency (EPA) announced the availability for public comment of the proposed methodology for the derivation of ambient water quality criteria for the protection of human health. The public comments were resolved in three phases.

First, comments relating to policy issues were resolved in an initial screening/disposition by Agency personnel. Second, a peer review workshop was conducted and involved Agency personnel, contractors, and recognized scientists. The group evaluated all issues pertaining to the derivation of criteria for non-carcinogens, and third, a similar workshop was held to review all issues relating to the derivation of criteria for carcinogens.

The following report presents the resolutions of the public comments by the EPA after considering the advice of the meeting attendees. While the EPA greatly appreciates the contribution of these individuals and acknowledges their substantial assistance in resolving many difficult questions, the EPA accepts full responsibility for the positions outlined in this document. (Note: Comments addressing similar issues were appropriately compiled and summarized under each issue.)

Comments Resolved in Initial Screening

Issue 1

Comment summary: The water quality criteria documents should provide information and/or guidelines for deriving standards from criteria.

Response: The water quality criteria documents contain information which will be useful in developing standards (e.g., current levels of exposure). However, in developing standards, many additional factors not directly related to criteria must be considered. It would be more appropriate to compile and to analyze this information as part of the standard-setting process rather than to include it in the criteria documents. Guidelines will be issued separately since the development of the standard includes use designation with a commensurate criteria value.

Issue 2

Comment summary: Water quality criteria should consider or be limited by technological achievability, cost/benefit analysis, limits of detection, and environmental fate.

Response: The distinction between criteria and standards must be recognized. For non-carcinogens, ambient water quality criteria are estimates of concentrations in water which will not result in either adverse human health effects (criteria based on toxicity) or unplesant taste or odor

(organoleptic criteria). For carcinogens, criteria are estimates of concentrations of individual compounds in water which will result in specified increases in the lifetime risk of developing cancer. By definition, these criteria exclude considerations of technological achievability, cost/benefit analysis, limits of detection, and environmental fate, as appropriate within the authority of The Clean Water Act [33 U.S.C. 1314(a)]. These factors are more properly considered in the standard-setting process.

Issue 3

Comment summary: The validity of a single criteria for all bodies of water is questionable. Criteria should be site specific an/or use specific.

Response: In the standard-setting process, criteria may be modified based upon site specific or use specific considerations.

Issue 4

Comment summary: Even if there is insufficient data, some criteria must still be developed for "highly hazardous compounds."

Response: If there is sufficient information to indicate that a compound is "highly hazardous," there should be sufficient information to derive a criteria. Conversely, if insufficient data are available, by definition no criteria can be derived.

Issue 5

Comment summary: Criteria should be derived only for persistent compounds or for compounds which present a clear hazard to humans.

Response: Criteria can be derived for any compound on which sufficient information is available. By definition, criteria are independent of persistence or current levels of exposure.

Issue 6

Comment summary: Criteria should be developed to protect terrestrial wildlife as well as humans and aquatic organisms.

Response: Because of the great number of diverse wildlife species and differences in their habitat, diet, and behavior, it is unlikely that a single criteria could be developed to protect all wildlife species from a given contaminant. The EPA is currently assessing possible approaches to developing a valid methodology for deriving wildlife criteria. Until a specific wildlife criteria methodology is developed, the proposed aquatic life and human health effects criteria should serve as interim levels for the protection of wildlife.

Issue 7

Comment summary: Criteria should be derived by an independent scientific panel and not by the EPA.

Response: The EPA has a legislative mandate to derive ambient water quality criteria and must accept the final responsibility for this process. However, the EPA has solicited the advice of many independent scientists in this effort. It should be noted that the consensus of the peer review committees has been considered and generally followed by the EPA. Nonetheless, the responsibility for the criteria rests solely with the Agency.

Issue 8

Comment summary: The ambient water quality criteria are not sufficiently protective of special groups at risk.

Response: In most cases, each document contains a specific section on special groups at risk. This is intended to serve as a notice to individuals or agencies using the criteria; that the derived criteria may not be sufficiently protective in all applications. If sufficient data are available, information in the section on special groups at risk could be used to modify the criteria during the standard-setting process.

Issue 9

Comment summary: Comments express concern with the failure of the criteria to specifically address possible toxicant interactions.

Response: The importance of toxicant interactions in the environment cannot be disregarded. Each document attempts to summarize the available data on such interactions. However, since the composition of toxicants is likely to vary substantially in different areas, a general approach modifying criteria based upon toxicant interactions is not available at this time. Further, the limitations of valid approaches for dealing with interactions in multi-toxicant mixtures should be recognized.

Issue 10

Comment summary: Because of the uncertainties involved in deriving criteria, the criteria should be limited to only one significant figure.

Response: The number of significant figures used to express the criteria is an admittedly arbitrary decision. The EPA recognizes the inexactitude of these numbers.

III. Comments on Non-Carcinogens

A. Criteria for Chemical Classes

Issue 1

Comment summary: Two basic approaches were taken in the documents on chemical classes when sufficient data were not available on all members in a class:

(a) Criteria were derived for individual chemicals on which sufficient data were available and no criteria were recommended for other chemicals in the class.

(b) A criteria was derived for all or some chemicals in the class based on toxicity data on one or a few members of the class.

Alternative "a" can be criticized for "allowing" contamination by "probably hazardous compounds" (reasoning by chemical analogy). Alternative "b" can be criticized for applying a general criteria to a specific compound for which data are not available.

What guidelines with justifications can be given for selecting either alternative? What other alternatives might be considered?

Response: The initial methodology did not adequately address the problems associated with deriving class criteria. The following section has been added to the methodology and serves as a useful guide in the criteria derivation process.

A chemical class is broadly defined as any group of compounds which are considered in a single risk assessment document. In criteria derivation, isomers are regarded as a chemical class rather than as a single compound. A class criteria is an estimate of risk/safety which applies to more than one member of a class, and involves varying degrees of extrapolation from available data on some members of the class to other class members on which sufficient data are not available to derive a compound-specific criteria (i.e., a criteria based on data solely on the specific chemical for which the criteria is derived).

A class criteria usually applies to each member within the class rather than to the sum of the compounds within the class. While the potential hazards of multiple toxicant exposure are not to be minimized, a criteria, by definition, most often applies to an individual compound. Exceptions may be made of complex mixtures which are produced, released, and toxicologically tested as mixtures (e.g., toxaphene and PCBs). For such exceptions, some attempt should be made to assess the effects of environmental partitioning different patterns of environmental transport and degradation on the validity of the criteria. If these effects cannot be

assessed, an appropriate statement of uncertainty should accompany the criteria.

Because relatively minor structural changes within a class of compounds can have pronounced effects on their biological activities, class criteria should be avoided. Whenever sufficient toxicologic data are available on a chemical within a class, a compound specific criteria for that chemical should be developed. Nonetheless, for some chemical classes, scientific judgment may suggest a sufficient degree of similarity among chemicals within a class to justify a class criteria applicable to some or all members within a class. Such a judgment should be influenced by a perceived risk to the human population if a class criteria was not derived.

The development of a class criteria should take into consideration the following:

(a) A detailed review of the chemical and physical properties of chemicals within the group should be available. A close relationship within the class with respect to chemical activity would suggest a similar potential to reach common biological sites within tissues. Likewise, similar lipid solubilities would suggest the possibility of comparable absorption and tissue distribution.

(b) The amount of qualitative and quantitative data for chemicals within the group should be examined. Obviously adequate toxicological data on a number of compounds within a group would provide a more reasonable basis for extrapolation than minimal data on one or two chemicals within a group.

(c) Similarities in the nature of the toxicological response to chemicals in the class provides additional support for the prediction that the response to other members of the class may be similar. In contrast, where the biological response has been shown to differ markedly on a qualitative and quantitative basis for chemicals within a class, extrapolation of a criteria to other members of that class may not be appropriate.

(d) Additional support for the validity of extrapolation of a criteria to other members of a class could be provided by evidence of similar metabolic and pharmacokinetic data, if available, for some members of the class.

Based on the above considerations, it may be reasonable to divide a chemical class into various subclasses. Such divisions could be based on biological endpoints (e.g., carcinogens/non-carcinogens), potency, and/or sufficiency of data (e.g., a criteria for some members of a class but no criterion for others). While no *a priori* limits can be placed on the extent of subclassification, each must be explicitly justified by the available data.

Class criteria, if properly derived and supported, can constitute valid scientific assessments of potential risk/safety and can be used in establishing appropriate standards. Conversely, the development of a class criteria from an insufficient data base can lead to serious errors in underestimating or overestimating risk/safety and should be rigorously avoided. Although scientific judgment has a proper if not totally explicable role in the development of class criteria, such criteria will be useful and defensible only if they are based on adequate data and scientific reasoning rather than intuition. The lack of data on dissimilarity cannot be used as the basis of a class criteria. Further, the definition of sufficient data on similarities in physical, chemical, pharmacokinetic, or toxicologic properties to justify a class criteria may vary remarkably depending on the degree of superficial structural similarity and the gravity of the perceived risk. Consequently, it is imperative that the criterion derivation section of each document in which a class criterion is recommended explicitly address each of the key issues discussed above and define, as clearly as possible, the limitations of the proposed criteria and the type of data necessary to generate a compound-specific criterion.

Class criteria should be corrected when sufficient data become available to derive a compound-specific criterion that protects against the biological effect of primary concern. The availability of a good subchronic study would not result necessarily in the abandonment of a class criteria based upon potential carcinogenicity.

The inability to derive a valid class criteria does not and should not preclude regulation of a compound or group of compounds based upon concern for potential human health effects. The failure to recommend a criterion is simply a statement that the degree of concern cannot be quantified from the available data and risk assessment methodology.

Issue 2

Comment summary: To what extent can "guilt by association" be used to derive a cancer-based criteria for a compound which has been tested for carcinogenicity with negative results [e.g., bis(2-chloroisopropyl) ether in the Chloroalkyl Ethers Ambient Water Quality Criteria Document].

Response: As stated in the response to Issue 1, "guilt by association" is only an extremely limited role in criteria derivation process.

B. Organoleptic Criteria

Issue 3

Comment summary: Whenever organoleptic criteria are derived, corresponding toxicity based criteria should be derived if possible.

Response: The Agency agrees. Since organoleptic criteria are not based on toxicologic information and have no direct relationship to potential adverse human health effects, both organoleptic and toxicity based criteria are provided whenever possible.

Issue 4

Comment summary: The quality of organoleptic criteria should be assessed in terms of experimental design and statistical analysis.

Response: The revised methodology recognizes the limitations of most organoleptic data:

With very few exceptions, the publications which report taste and odor thresholds are cryptic in their descriptions of test methodologies, number of subjects tested, concentration/response relationships, and sensory characteristics at specific concentrations above the threshold. Thus the quality of the data is usually worse than the toxicological data used for the setting of other criteria. Consequently, a clear critical evaluator of the available data on a compound's organoleptic characteristics should appear in the criteria document.

Issue 5

Comment summary: Criteria based on organoleptic properties should not be considered equal to criteria based on toxicologic effects.

Response: The revised methodology makes a clear distinction between organoleptic and toxicity based criteria. The use of the criteria in the regulatory process should reflect an appreciation of this distinction.

C. Naturally Occurring Compounds

Issue 6

Comment summary: Background levels should be defined in terms of the quality of the data base and geographical/seasonal variations.

Response: The documents summarize data on background levels of naturally occurring compounds and include information on seasonal and/or geographical variation when available.

Issue 7

Comment summary: A distinction should be made between natural and anthropogenic background.

Response: An attempt is made, with extreme difficulty, in the exposure section of the documents to differentiate between natural and anthropogenic background. However, background levels cannot be used directly to modify the criteria. By definition, criteria should not consider current levels of exposure but are estimates of safe level or incremental risk level exposures. Background levels, both natural and anthropogenic, should be considered if the criteria are used to promulgate standards.

Issue 8

Comment summary: What is the minimum data base needed to define a compound as essential?

Response: As indicated in the revised methodology, elements will be accepted as essential if the National Academy of Sciences (NAS) Food and Nutrition Board or a comparably qualified group declares them as such. Elements not yet determined to be essential, but for which supportive data on "essentiality" exists, were recommended to be reviewed by a joint EPA/NAS committee.

Issue 9

Comment summary: How can essentiality be used to modify a criteria?

Response: The following additions have been made to the revised methodology in response to this question:

In order to be useful in modifying toxicity/carcinogenicity based criteria, essentiality must be quantified either as a recommended daily allowance (RDA) or minimum daily requirement (MDR). These levels must be compared to estimated daily doses associated with the adverse effect of primary concern. The difference between the RDA or MDR and the daily doses causing a specified risk level for carcinogens or acceptable daily intake (ADI) for non-carcinogens defines the "window" of daily doses from which the criteria should be derived.

Because errors are inherent in defining both essential and maximum tolerable levels, the criteria should be derived from dose levels near the center of such a dose range. The decision to use either the MDR or RDA will be guided by the size of the window and the quality of the essentiality and toxicity estimates.

The modification of criteria by consideration of essentiality must include all routes of exposure. If water is a significant source of the MDR or RDA, the criteria must allow for attainment of essential intake. Conversely, even when essentiality may be attained from non-water sources, standard criteria derivation methods may be adjusted if the derived criterion represents a small fraction of the ADI or MDR. On a case-by-case basis, the modification in the use of the guidelines may include the use of different safety factors for non-carcinogens or other modifications which can be explicitly justified.

D. Use of NOAELs/NOELs

Issue 10

Comment summary: NOELs and related effect terms should be defined more clearly in the methodology.

Response: In the revised methodology, the following additions have been made to clarify the use of these terms:

In developing guidelines for deriving criteria based on non-carcinogenic responses, five types of response levels are considered:

NOEL—No-Observed-Effect-Level
LOEL—Lowest-Observed-Effect-Level
NOAEL—No-Observed-Adverse-Effect-Level
LOAEL—Lowest-Observed-Adverse-Effect-Level
FEL—Frank-Effect-Level

In the above terms, adverse effects are defined as any effect resulting in functional impairment and/or pathological lesions that may affect the performance of the whole organism, or which contributes to a reduced ability to respond to an additional challenge. The word lowest refers to the incidence of the effect in the tested population. It should be noted that LOELs, NOAELs, and LOAELs refer to exposure levels or dosage zones which are experimentally defined by upper and lower exposure levels. NOELs and FELs, however, are not defined at the lower and upper exposure levels, respectively.

Issue 11

Comment summary: Considerations of experimental design should be more explicitly/quantitatively considered in the criteria derivation process.

Response: The development of a rigid system for considering experimental design in criteria derivation would limit the use of scientific judgment. The section of the methodology dealing with the derivation of toxicity based criteria has been extensively revised to allow for the maximum use of scientific judgment in selecting safety factors based on both the quality of the individual study and the weight of the supporting scientific data.

E. Safety or Uncertainty Factors

Issue 12

Comment summary: Can the guidelines for applying safety factors be clarified or developed in greater detail to minimize inconsistencies without impairing scientific judgment?

Response: The following additions have been included in the methodology to allow for the use of greater judgment in the application of safety factors, while also requiring more explicit justification for the use of any uncertainty factor:

The justifications for the various safety factors can become very restrictive if they are not employed with care and judgment. This is the case especially in those instances where the data do not completely fulfill the conditions for one category of uncertainty factor and appear to be intermediate between two categories. Given the uncertainties in the entire process, it is more appropriate to set the operative uncertainty factor at some intermediate value on a logarithmic scale (e.g., 32, being halfway between 10 and 100 on a logarithmic scale). If intermediate values for uncertainty factors are more representative of actual conditions, then they are used.

In the selection of the uncertainty factor approach, "no indication of carcinogenicity" is interpreted as the absence of carcinogenic data from animal studies or human epidemiology. Short-term carcinogenicity screening tests are considered in the criteria documents, and are used in the derivation of numerical criteria and are used to rule out the uncertainty factor approach.

Because of the high degree of judgment involved in the selection of a safety factor, the criteria derivation section of each document must provide a detailed discussion and justification for both the selection of the safety factor and the data for which it is applied. This discussion should reflect a critical review of the total data base. Factors to be considered include: number of animals tested, parameters tested, species tested, quality of controls, dose levels, route, dosing schedules, etc. An effort should be made to differentiate between coherent results which form a toxicologically valid data base and data which may be spurious in nature.

Issue 13

Comment summary: What, if any, safety factor should be used when deriving criteria from a threshold limit value (TLV).

Response: The safety factor used when deriving criteria from a TLV must

depend on the quality of the data base on which the TLV is based, considerations of uncertainties involved in extrapolating data from inhalation to oral exposures, and the quality of the additional supporting data.

F. Related NOAEL Issues

Issue 14

Comment summary: Can/should concentration response curves representing a "full range of effects" be used in deriving criteria?

Response: No available system for utilizing concentration response curves in representing a full range of effects for deriving criteria has been developed. If such a system does become available, it will be assessed by the Agency.

Issue 15

Comment summary: When more than one method is available to derive a non-carcinogen criteria (e.g., 2-year chronic, 90-day, TLV), can guidelines be given for selecting the most appropriate method?

Response: As indicated in the revised methodology, criteria can be based on several different types of data (e.g., studies on humans or experimental animals, subchronic or chronic exposure periods, oral or inhalation exposure routes, TLVs or similar standards). Specific guidelines for selecting a particular study or approach have not been recommended because of the many judgmental factors which are involved. As indicated in the methodology, the criteria derivation section must specifically state the reasons for selecting the approach and study used to derive the criteria.

Issue 16

Comment summary: The approach used to derive criteria for non-carcinogens may not adequately address the question of whether children are at greater risk than adults.

Response: When specific data are available on women or children as groups at increased risk, it should be stated in the document and discussed in the criteria derivation section, but should be used to modify the criteria only if sufficient specific data are available. This is a highly judgmental decision which must be made on an individual case.

Issue 17

Comment summary: Criteria based on carcinogenic effects might not be adequate to protect humans from mutagenic, teratogenic, or other toxic effects.

Response: With very few exceptions, criteria based on carcinogenicity are probably protective for other toxic effects. However, alternative criteria can be derived based on non-carcinogenic effects on a case-by-case basis if there is any doubt of the level of protection offered by the cancer based criteria.

G. Alternative Approaches to the Development of Criteria for Non-Carcinogens

Issue 18

Comment summary: Is there a reasonable way to use multiple NOEL/NOAELs to derive criteria?

Response: The revised methodology clearly indicates that all toxicity must be considered in deriving criteria and multiple NOELS/NOAELs are used. A detailed mathematical approach using multiple NOEL/NOAEL data has not been developed or accepted by the scientific community.

Issue 19

Comment summary: Is there a reasonable way to use dose/response data to derive criteria?

Response: Mathematical models for deriving non-cancer based criteria are available. However, they have not gained wide acceptance in human risk assessment. Until various models have been reviewed in greater detail, the Agency uses the current approach, based on that recommended by the National Academy of Sciences, as the most appropriate.

Issue 20

Comment summary: Confidence intervals or a range should be used in deriving criteria.

Response: A workable method for using confidence intervals in deriving non-cancer based criteria has not been developed. Given the many uncertainties involved in this process, the use of confidence intervals could be misleading in simply considering problems in statistical variation without considering problems in species to species conversion. Safety factors are an accepted procedure and are used to consider both problems in statistical variability as well as problems in species to species conversions and individual susceptibility.

H. Exposure

Issue 21

Comment summary: Should non-cancer criteria be based on all sources of exposure because they are derived from estimates of ADIs (acceptable daily intake) which define *total* daily acceptable doses for man?

Response: The methodology has been revised so that estimates of total exposure can be considered in deriving criteria. Estimates of water and fish consumption are used to derive the criteria. However, the criteria levels can be modified by considering all routes of exposure in the standard-setting process. This approach may be particularly desirable because exposure conditions will probably vary markedly on a regional basis.

Issue 22

Comment Summary: If sufficient data are not available on all sources of exposure, can any reasonable assumptions be made to factor in all sources of exposure or can/should an additional "uncertainty" factor be used?

Response: When no reasonable estimate can be made of contributions from non-fish diet and from air, it can be assumed that one-half of the exposure comes from water and fish and one-half comes from other sources. This is equivalent to using an additional safety factor of 2. It is recognized that the inability to quantify all sources of exposure adds an additional element of uncertainty to the criteria.

I. General Issues

Issue 23

Comment Summary: With the exception of recommending "good scientific judgment," can specific guidelines be given for accepting or rejecting a study or set of studies as a data base for criteria derivation?

Response: Specific guidelines cannot be given for accepting or rejecting studies. Scientific judgment must be exercised in view of the magnitude of the total evidence on the chemical or chemicals under consideration. Chronic data and appropriate exposure routes are most desirable.

Issue 24

Comment Summary: Is there a need to individualize the criteria derivation process so that the "nature of the toxic agent and its mechanism of action" can be more explicitly considered? If so, how can this be accomplished?

Response: The criteria derivation process does consider as specifically as possible the nature of the toxic agent and, when known, the mechanism of action.

Issue 25

Comment Summary: Is the Stokinger-Woodward model adequate for converting inhalation dose data to "equivalent oral doses," or should a more sophisticated approach be used?

Response: The derivation of water quality criteria from inhalation data is an admittedly tenuous process. The

following guidelines have been added to the methodology:

Estimating equivalencies of dose/response relationships from one route of exposure to another introduces an additional uncertainty in the derivation of criteria. Consequently, whenever possible, ambient water quality criteria should be based on data involving oral exposures. Even with oral data, differences in dosing schedules and vehicles can be problematic. If oral data are insufficient, data from other routes of exposure may be used in deriving water quality criteria.

Inhalation data, including TLVs or similar values, are the most common alternative to oral data. Estimates of equivalent doses can be made on the basis of extensive pharmacokinetic data for oral and inhalation routes, on the basis of measurements of absorption efficiency from ingested or inhaled chemical, or on the basis of comparative excretion data when the metabolic pathways can be established to be equivalent after oral or inhalation dosing. When sufficient pharmacokinetic data are available, the use of accepted pharmacokinetic models provides the most satisfactory approach for dose conversions. However, if the pharmacokinetic data are marginal or of questionable quality, pharmacokinetic modeling is inappropriate and may result in an artifical sense of exactitude.

The Stokinger and Woodward (1958) approach, or similar models which are based on assumptions of breathing rate and absorption efficiency, can be used as alternatives when data are not sufficient to justify pharmacokinetic principles. Consequently, in using the Stokinger and Woodward or related models, the uncertainties inherent in each of the assumptions and the basis of each assumption should be clearly stated in the derivation of the criteria.

The use of data involving other routes of exposure to derive water quality criteria should not be ruled out. However, as with inhalation data, an attempt should be made to use accepted toxicologic and pharmacokinetic principles to estimate equivalent oral doses. If simplifying assumptions are used, their bases and limitations must be clearly specified.

Because of the uncertainties involved in extrapolating from one route of exposure to another and the consequent limitations that this may place on the derived criteria, the decision to disallow such extrapolation and recommend no criterion is highly judgmental and must be made on a case-by-case basis. Such a decision should balance the quantity and quality of the available data against a perceived risk to the human population if no criteria is derived.

Issue 26

Comment Summary: Can/should criteria be qualitatively or quantitatively ranked in terms of their scientific strength of validity? How could such a ranking system be developed?

Response: The Agency is presently assessing the quality of the data base supporting individual criteria. This will eventually result in the development of a ranking system of all the priority pollutants.

IV. Response to Public Comments on Methodology to Derive Water Quality Criteria

The Carcinogen Assessement Group (CAG) and the Environmental Criteria and Assessment Office-Cincinnati (ECAO-Cin.) of the U.S. Environmental Protection Agency (EPA) has reviewed in detail the public comments on EPA's methodology to derive water quality criteria for carcinogens. Since the majority of the comments are concerned with the low-dose extrapolation procedure and since they are closely related to each other, an appendix is presented which summarizes our new procedure to derive water quality criteria and the rationale for selecting the procedure and compares the new with the old procedure. Much of the criticism has been directed toward utilization of the one-hit linear model for estimation of the risk. After considerable input by a peer review of outside scientists, the multistage model developed by Kenneth Crump has been adopted in place of the one-hit model extrapolation. The Appendix describes the new multistage hit model. Further responses to the individual comments are being presented below.

A. The One-Hit Model

Issue 1

Comment summary: Several comments criticize the one-hit model as arbitrary, inappropriate, simplistic, unrealistic, inaccurate, not universally accepted, and/or overly conservative.

Response: The Agency has adopted a new procedure for deriving water quality criteria which is conceptually similar to, but operationally more systematic than the one-hit procedure used previously by the Agency. Although the criteria calculated by the new procedure are not appreciably different than those calculated by the old procedure as demonstrated in the appendix, most of the general criticisms do not apply to the new procedure.

Issue 2

Comment summary: Comments pointed out that the EPA has declined to use the one-hit model under the federal pesticide laws for heptachlor and chlordane.

Response: The commentor is correct that the one-hit model was not used in the chlordane-heptachlor suspension hearings in 1975. However, in the cancellation hearings, which were held after the formation of the Carcinogen Assessment Group and the adoption by the Agency of the Interim Cancer Assessment Guidelines and in the proposed water quality criteria, one-hit extrapolation model was used for risk estimation. In the current final water quality documents the "linearized" multistage model is used; the comparison between these two approaches in the appendix to those comments shows that the chlordane and heptachlor data have the largest upward curvature in the dose-response curve of all the carcinogens in the water quality list. For this reason the new approach reduces the risk for chlordane and heptachlor more than for the other compounds. This example shows how the new extrapolation procedure compensates for the "overly conservative" results of the one-hit approach in cases where the dose-response data is sharply concave upward at low doses.

Issue 3

Comment summary: The EPA's choice of this model because ". . . it gives greater risk estimates than other plausible models" (page 15978 of March 15, Federal Register) was criticized as being a policy/political/social statement rather than a scientific defense.

Response: See the appendix for reasons for selecting linear, non-threshold models.

Issue 4

Comment summary: The statement that this model was endorsed by IRLG (1979) was felt to have limited meaning because this document has not yet been reviewed and because the document is merely a reiteration of policy.

Response: The model was not selected on the endorsement of IRLG. See appendix.

Issue 5

Comment summary: In the methodology (page 15978, column 1, first full paragraph of the March 15, Federal Register), this model is scientifically defended as being consistent with three basic concepts in chemical carcinogenesis:

a. The Linearity of the Dose-response Curve for Mutagens—This is challenged on the following points:

The shape of the dose response curve in the low dose region cannot be determined.

Not all assay systems give linear dose-response patterns.

Some Ames tests are linear because the liver microsomes are added in a fixed amount and thus ". . . the laws of first order kinetics require a linear response to the variation in concentrations of the test substance as it is mediated by the activator."

b. Chemicals which are Mutagens are Likely to Induce Cancer—This is challenged on the basis that not all mutagens cause cancer.

c. Epidemiology Studies on Radiation, Cigarettes, and Aflatoxin show a Linear Dose-response Pattern—This is challenged on the following points:

Radiation carcinogenicity cannot be applied to chemical carcinogenicity because they act by different mechanisms.

Not all radiation dose-response data is linear.

Smoking data are compounded by difficulties with cocarcinogens and other exposures.

Aflatoxin data rely purely on estimated exposures.

Response: (a) The commentor points out that even in mutagenesis test systems there is a level of mutagenic response that is too small to be detected and that below this level the shape of the dose-response curve cannot be measured. While this is true, the Agency's point is that the mutagenesis data available are fundamentally consistent with a linear no-threshold mechanism of action. Another commentor has misinterpreted the mutagenesis dose-response data. As presented by the original authors, the data show some residual mutagenic activity at zero dose. This is interpreted erroneously as being a threshold below which no response occurs. Another commentor supports the Agency's contention that the mutagenesis dose-response relationship is linear by giving a possible explanation for the linearity.

(b) The fact that chemicals which are mutagenic are "likely" to induce cancers does not imply that "all" mutagens cause cancer. Furthermore, those mutagens which were not shown experimentally to be carcinogenic could not be accepted unequivocally as non-carcinogenic because of the uncertainty in the study outcome.

(c) Both chemicals and radiation cause DNA damage and subsequent interference with the normal functioning of DNA, although the mechanisms for causing this damage are different for radiation and chemicals.

Issue 6

Comment summary: Several comments stated that the possibility of thresholds for at least some chemical carcinogens is not unreasonable, should be addressed in greater detail and/or cannot be resolved at this time. The possibility of assuming a threshold was recommended for the following compounds: chloroform, PCBs, acrylonitrile, hexachlorocyclohexane, chlorinated benzenes, and chlorinated ethanes.

Response: Currently there is no satisfactory method for estimating the low-dose carcinogenic risk to "epigenetic" chemicals. Until the mechanisms for such action are understood on a case-by-case basis to the point of being able to justify a specific extrapolation procedure, the linear, no-threshold concept will be assumed to be valid. The "linearized" multistage approach now used result in lower risks than the older "one-hit" approach for compounds having a sharp upward curvature.

For the specific chemicals referred to in Issue 6, no evidence was presented in support of a carcinogenic threshold dose except for chloroform. Commentors state that chloroform induces an increased rate of cell proliferation, which they implicitly equate with carcinogenesis, at high doses because of a cytotoxic response which is unrelated to direct DNA interaction and which therefore is not expected to occur at low doses. Three pieces of evidence are cited in support of that position: (a) chloroform is not mutagenic in the Ames tests; (b) at doses below 15 mg/kg/day, mice show no excess rate of DNA synthesis in kidney and liver tissue. This excess is expected for a cytotoxic response leading to cell proliferation; (c) Roe et al (1979) on the basis of responses in four strains of mice, has established a no-carcinogenic effect level of 17 mg/kg/day, whereas the positive NCI experiment used by EPA for the water criterion was carried out at 200–400 mg/kg/day.

Before the existence of a threshold for chloroform can be established several issues need to be resolved: (a) are the no-effect levels in the DNA synthesis studies and in Roe's observations real phenomona or only artifacts occurring simply because the limit of detection in these studies was being reached? (b) The relation between the cellular proliferation, which is alleged to be manifested by increased DNA synthesis, and carcinogenesis is unclear, since in the mouse strains used by NCI kidney tumors do not occur and liver tumors do, whereas in the experiments cited by a commentor both liver and kidney exhibit DNA synthesis.

Issue 7

Comment summary: A distinction should be made between genetoxic and epigenetic carcinogens based on mutagenicity data. These comments imply that a threshold model would be more appropriate for epigenetic carcinogens.

Response. While it is true that most carcinogens do interact with DNA, there are some compounds, such as phorbol esters in mouse skin studies and phenobarbital in rat liver, which are incomplete carcinogens by themselves, but require another substance to initiate or promote their action. In these studies the effects are unrelated to DNA interactions and apparently involve important recovery processes. This newly-developing field is not yet well enough understood to justify the use of a particular dose-response extrapolation model.

Issue 8

Comment summary: Another group of comments vigorously opposed the non-threshold assumption used in the one-hit model. Criticism of the non-threshold assumption were most extensively articulated by commentors which contended that the non-threshold assumption is:

Contrary to experience and logic, to what is known of biological systems, and to existing scientific data and is a product of the desire to obtain a simple and easy-to-use method for criteria derivation.

A related comment contended that thresholds are apparent for mutagens and therefore—given the presumed relationship of carcinogenicity to mutagenicity—thresholds should be postulated for carcinogens.

Response: Commentors state that the linear non-threshold model is: (a) contrary to experience and logic; (b) contrary to what is known about biological systems; (c) contrary to existing scientific data and (d) an approach based on faith that could not be disproved by any facts.

(a) The linear non-threshold model does not imply, as suggested by a commentor, either that (a) cancer is inevitable in the general public or in heavily exposed industrial workers or that (b) all substances are carcinogenic. It simply states that the probability of a person getting cancer is proportional to the amount of carcinogen to which he is exposed.

First order reaction processes are ...non in biological systems especially ...mutagenesis.

(c) Dr. Bingham's article did not ...vocate a sigmoid dose-response curve preference to a linear curve, as stated ... the commentor. She stated that ...veral environmental factors can alter ...e dose-response relationship, and ...ould thereby change the curve ...hichever way it was described. In fact, ...r main point was that "until we ...derstand more about the primary ...rcinogenic insult and its progression, ...edicting or estimating thresholds is ...ky." The Agency agrees with this ...nclusion.

(d) The Agency agrees that it would ... extremely difficult to use negative ...idemiology data as proof that a ...rcinogenic threshold exists for a ...mpound having positive animal ...sults.

...ue 9

Comment summary: Several ...mments critized the one-hit model ...cause it does not fit some ...perimental data as well as other ...dels. This was illustrated for ...ptachlor, chlordane, and aflatoxin and ...lorinated ethanes.

Response: The new extrapolation ...thod overcomes the difficulty in ...ting the model to the data because the ...ltistage model has enough flexibility ...fit any montonically increasing dose-...sponse relationship. See also the ...sponse to Issue 16.

...ue 10

Comment summary: The application ...the model was also criticized because ...disregards data at all but one dose ...el and fails to consider the results of ...er experiments.

Response: The new procedure does ...t have these shortcomings. See ...pendix.

...ue 11

Comment summary: The highest ...ency factor to the exclusion of all ...er data should not be used in ...erating criteria because this process ...s not involve maximum-likely risk ...imates.

Response: In judging which of several ...mal studies to use as the basis for the ...ntitative risk estimate, the quality of ...h study is considered as well as the ...nerical slope factor. As explained in ... preamble, an experiment with a ...all number of animals is rejected in ...or of a larger experiment if the two ...e a similar dose-response ...tionship. A similar rejection is also ...de if an experiment is judged to be ...eliable for other reasons. Because of the strain, species, and sex differences, it is considered improper to calculate an average response across all animal species and designate this average as the carcinogenic potency for animals in general.

Issue 12

Comment summary: ". . . no experiment, however large and well run, could ever reduce these estimates (criteria)."

Response: In judging which of several animal studies to use as the basis for the quantitative risk estimate, the quality of each study is considered as well as the numerical slope factor. As explained in the preamble, an experiment with a small number of animals is rejected in favor of a larger experiment if the two have a similar dose-response relationship. A similar rejection is also made if an experiment is judged to be unreliable for other reasons. Because of the strain, species, and sex differences it is considered improper to calculate an average response across all animal species and designate this average as the carcinogenicity potency for animals in general.

Issue 13

Comment summary: The EPA method is insensitive to reproducibility of the results, results at lower doses, and the number of animals per dose group.

Response: In judging which of several animal studies to use as the basis for the quantitative risk estimate, the quality of each study is considered as well as the numerical slope factor. As explained in the preamble, an experiment with a small number of animals is rejected in favor of a larger experiment if the two have a similar dose-response relationship. A similar rejection is also made if an experiment is judged to be unreliable for other reasons. Because of the strain, species, and sex differences, it is considered improper to calculate an average response across all animal species and designate this average as the carcinogenic potency for animals in general.

Issue 14

Comment summary: Several examples are given of the failure of the one-hit model to predict cancer rates in humans based on epidemiologic studies:

Analyses of data on: chloroform, carbon tetrachloride, tetracholoroethylene, aflatoxin, chlordane, arsenic, and beryllium.

In a summary of analyses of DDT, dieldrin, and aflatoxin, it is indicated that the one-hit model predicts an incidence of 153,000 liver cancers per year but that the observed response rate from all chemicals in only 3,000 to 4,000 per year. A similar analysis is made of pollution exposure-cancer rates in the Sacramento River area.

Response: For chloroform, carbon, tetrachloride, and tetrachloroethylene the analysis assumed that all of the workers were exposed at the TLV levels for their entire lifetime. In reality most workers are not exposed continuously to levels as high as the TLV and most work for only a few years at these jobs. This procedure overestimates the average lifetime exposure by at least a factor of 10 and the risk estimates for the workers are too high because of exposure assumptions used by the commentor rather than solely because of an overestimated slope factor.

For aflatoxin the commentor showed that the multistage model fits the observed human data more closely than the one-hit model. Therefore, that analysis partially justifies the revised procedure, although this compound is not on the water quality list.

The criterion for arsenic was based on human data, which was linear with dose. However, none of the negative epidemiology studies in areas with high drinking water levels of arsenic was inconsistent with the model developed on the basis of the Taiwan skin cancer data.

Commentors estimated that the annual number of cancer cases caused by beryllium intake is about 14,000. They gave no reason why this number is considered excessive considering that 400,000 cases per year are observed from all causes.

Issue 15

Comment summary: Based on the above types of analyses, several comments recommended that epidemiologic data be used to test and/or modify risk estimates.

Response: The Agency agrees that good epidemiological data should be used to estimate or modify risk estimates. The Agency always preferred using epidemiological data to the animal data in deriving water quality criteria.

Issue 16

Comment summary: Some comments suggest that selection of a particular model should be left open and subject to the nature of the experimental data and epidemiologic or metabolic information.

Response: The Agency does not agree that the selection of a particular model should be left open and subject to the nature of the experimental data for the following reasons. When behavior of the dose-response curve at low doses is not sufficiently understood, it is more appropriate to predetermine the low-

dose extrapolation model. Considering the fact that all the mathematically analytic functions such as most of the parametric dose-response curves could be approximated by polynomials which are dominated by the higher order terms in the high-dose range, whereas they are vanishingly small in the low-dose regions it is not surprising to see that different dose-response models could fit well a set of high dose data while their low-dose extrapolations differ drastically. Therefore, the selection of the extrapolation model should be based on knowledge of carcinogenic mechanisms (even though limited and debatable) rather than being determined solely by the high dose behavior of the dose-response curve.

Issue 17

Comment summary: Other comments suggested that the one-hit model should be used only in the absence of data suggesting that other models give a better fit.

Response: See response to Issue 16 and the appendix.

Issue 18

Comment summary: Two comments recommend that several models used for analysis along with appropriate confidence intervals would more objectively reflect the state of scientific knowledge.

Response: The inclusion of several arbitrary models in order to get a range of risk estimates would add no additional scientific information while at the same time would create confusion and thereby undermine the utility of risk estimates. The model chosen by the Agency is regarded as giving a plausible upper limit to the risk.

Issue 19

Comment summary: A general discussion of alternative models is given in some of the comments. Specific models recommended include: Logistic; Probit; Multi-hit; Mantel and Bryan; Weibull; and Pharmacokinetic.

Response: The inclusion of several arbitary models in order to get a range of risk estimates would add no additional scientific information while at the same time would create confusion and thereby undermine the utility of risk estimates. The model chosen by the Agency is regarded as giving a plausible upper limit to the risk.

B. Use of Confidence Intervals

Issue 20

Comment summary: Confidence intervals or a range should be used in deriving criteria.

Response: The Agency feels that the statistical confidence intervals should not be used to express the range of uncertainty of the criteria because this range does not include major uncertainties which are not quantifiable, such as species differences in metabolism, diet, target organ specificity, and other biological variables.

C. Species Conversion Factor (W_H-W_A)⅓

Issue 21

Comment summary: Comments suggested that this factor may not be appropriate for carcinogens because: (a) DNA repair rates appear to be inversely proportional to body weight, and (b) mixed-function oxidase activity, which may activate carcinogens, is higher in rodents than in man. Examples were given indicating that man is less sensitive than experimental mammals to chloroform, aflatoxin, and vinyl chloride.

Response: Although some commentors discussed reasons why the species conversion factor, (70/W)⅓, may not be appropriate for particular compounds, no suggestion was made for an alternative method which would be valid in general. Commentors suggested that mixed-function oxidase activity is lower in humans than in rodents and that humans metabolize chloroform less completely than animals, but facts like these, even if quantified would have uncertain implications to carcinogenic potency in general because increased metabolic activity could both enhance carcinogenic potency by "inactivating" the agent.

The fraction of a compound (e.g. chloroform) unmetabolized may have no relation at all to the amount of active metablite formed. In the general method, the cube root factor is intended to account only for the body size difference between animal species as it relates to the availability of the chemical to the body tissues. Any specific knowledge available on metabolism differences would have to be incorporated as an additional factor if it could be directly related to cancer incidence. In general, mixed-function oxidase activity has no clear relation to cancer occurrence, therefore, cannot be included in the general approach.

The best apporach for checking the validity of the species conversion factor is to correlate carcinogenic potency of agents in animals with that in humans where suitable information is available. This was done in a preliminary fashion by Messelson (quoted by one commentor) and is currently being investigated by the Agency.

Issue 22

Comment summary: Data on comparative metabolism should be used, whenever possible, to modify the risk estimate.

Response: See Issue 21 for response to chloroform metabolism issue. The Agency acknowledges that species differences in metabolism should be considered in all cases where the data can be interpreted as being relevant to carcinogenicity. In the methodology description the appropriate place to incorporate this information is in the factor r, called the absorption fraction.

D. Time-To-Tumor Data

Issue 23

Comment summary: Some comments stated that the EPA's modification of the one-hit model does not consider the time-to-tumor concept.

Response: The time-to-tumor concept was incorporated in the one-hit procedure by using the model $P=1-\exp[-bd\,t^3]$ where t is the average fraction of a lifetime the tumor was observed and is also incorported into the current approach. If sufficiently well defined time-to-tumor data are available, a more refined model would be used.

Issue 24

Comment summary: Other comments contended that, because of the relationship between dose and latency, even potential carcinogens will not induce tumors in a normal lifespan. Examples were given for beryllium and arsenic.

Response: The arguments given in this comment do not invalidate the criteria which are associated with a lifetime risk of 10^{-5}. The arguments given in the comment proceed as follows:

Let F(d,t) be the probability of cancer by age t at exposure d. F is a monotonic increasing function of both variables t and d. Let d_o be the exposure associated with the lifetime risk of cancer 10^{-6} obtained by solving for d from the equation $F(d,t) = 10^{-6}$ and $t = 70$ which is taken as the average lifespan. Based on the arsenic risk assessment by the CAG the comment argues that at exposure $d_o = 0.002\ \mu g/liter$ (where d_o is associated with a lifetime risk of 10^{-6}), the median age would be 2,636 years before cancer can occur, where 2,636 is obtained by solving for t from the equation $F(d_o,t) = 0.5$.

Therefore, if the water concentration is 0.002 μg/l the risk at 70 years is 10^{-6} and at 2,636 years it would be 0.5. These

are not inconsistent statements, as implied by the commentor.

Issue 25

Comment summary: One comment suggested that studies in which t is less than 0.75 may not be useful because of insufficient time for tumor development.

Response: The t^3 factor is necessary when the carcinogenic response is so strong that the animals die prematurely of tumors. This is true regardless of whether the median time of death from tumors is greater or less than three-fourths of their natural lifespan.

Issue 26

Comment summary: Another comment raised questions about the experimental difficulties of Druckery's work in precisely determining time-to-tumor development and the need to correct time-to-tumor data for the degree of malignacy of the tumor.

Response: The time-to-tumor data is used only when there was an early terminal sacrifice. In this case the full spectrum of tumor development is observable histologically and the difficulty of observing the precise time of tumor development is not encountered.

E. Mutagenicity Data

Issue 27

Comment summary: Mutagenicity data should be given greater weight to determine potential carcinogenicity especially when mammalian bioassays or epidemiology data are lacking.

Response: See response to Issue 28.

Issue 28

Comment summary: The commentor describes a method for using results from short-term tests, such as the Ames test or the hamster embryo *in vitro* transformation test, to perform quantitative carcinogenicity risk assessment.

Response: The Agency does not regard results from short term mutagenicity tests, even those from a test battery using several organisms, equivalent to chronic whole animal bioassays for carcinogenicity because of the inherent differences between the test systems utilized (i.e., bacteria and cell cultures versus whole animals, in which all the metabolic, distribution and excretion systems of the body are intact). Until correlations between the carcinogenicity and mutagenicity of agents become better understood and more widely accepted, and until the data base is more extensive, the Agency is not justified in making quantitative assessments of carcinogenicity based solely on mutagenicity test results and structure activity relationships. In decisions regarding the carcinogenicity of agents, the Agency currently uses short term bioassay tests only to support equivocal findings of long term animal bioassays and human studies.

F. Epidemiology Data

Issue 29

Comment summary: Epidemiology data on societies other than the U.S.A. should not be used because of "dissimilar and possibly controlling variables."

Response: The CAG feels that epidemiological data on societies other than the U.S.A. population can be used as long as care is taken in interpreting and using the data.

Issue 30

Comment summary: Citing criteria for arsenic and cadmium, the comment states that: "Valid epidemiological studies exploring a cause-and-effect relationship between exposure to a substance and disease must avoid a number of flaws: bias, confounding factors, and the confusion of chance associations with casual relationships. The epidemiological studies used by the Agency in criterion formulation fail to avoid these flaws."

Response: While nearly every epidemiologic study contains flaws in the scientific sense, a regulatory agency must interpret all data available, making judgments as to whether the studies were too flawed for proper conclusions. In determining the carcinogenicity of a substance, the Agency is sensitive to the need to find human populations who have been exposed to other agents also. The appearance of rare types of cancers and/or a dose-response trend, however, often provide(s) very positive evidence of carcinogenicity. Such is the case with the Taiwan drinking water survey. Here, where artesian well water with a high concentration of arsenic has been used for more than 60 years, a high correlation between amount of arsenic and skin cancer was found. In addition, the pre-cancerous skin conditions were pathonomic of arsenic exposure, so that there was little chance that the cancers were caused by another agent. Furthermore, the skin cancer is of a rare form that was virtually unknown in parts of Taiwan where the drinking water arsenic content was small. In addition, a positive association between arsenic level in drinking water and the prevalence of skin cancer has been reported in at least three other areas in the world.

Cadmium is an unusual situation in that five independent populations showed an excess of prostate cancer. Even though each study is inconclusive by itself for the reasons cited, a chance occurrence of this finding is exceedingly unlikely.

While the effect of many possible confounding factors, especially concomitant exposure to unknown chemicals, cannot be accurately determined, the Agency has the responsibility of estimating criteria levels with the best information available.

G. Qualitative Determination of Carcinogenicity

Issue 31

Comment summary: The commentor states that: "A substance is currently considered to be carcinogenic if it produces a statistically significantly higher than normal incidence of tumors in treated animals in a single test. Such a result is inconclusive, because of the problems of false positives.

Response: In establishing a false negative rate of $P<0.05$ the commentors correctly point out that the false positive rate is rather high. However, the careful review of other information about the compound reduces the effective false positive rate.

Issue 32

Comment summary: The decision to label a compound "a suspect human carcinogen and therefore a potential human carcinogen" based on tumorigenicity in experimental mammals has not been validated.

Several comments from the initial publication of the methodology made a similar criticism.

Response: Among public health authorities it is widely accepted that the positive results in chronic animal bioassays indicate that the agent poses a potential risk for human carcinogenicity. This attitude is thoroughly summarized in the IRLG report (Jour. Natl. Cancer Inst. 63: 241, 1979). In addition, a review by Tomatis (Am. Rev. Pharmacol. Toxicol. 79: 511, 1979) emphasized the value of rodent bioassays in predicting human carcinogenic risk.

Since 1976, (41 FR 21402) the EPA has been following the same regulatory philosophy in evaluating carcinogenic hazards. Therefore, contrary to the comments, the EPA has not been acting unilaterally without adequate public notice.

Issue 33

Comment summary: The commentor quotes a WHO publication: "It would be unwise to classify a substance as a

carcinogen solely on the basis of a species or strain-specific increased incidence of tumors of a kind that occur spontaneously with high frequency."

Response: The CAG agrees partially with the comment. However, even if the spontaneous incidence is high, a statistically significant enhancement of the tumor incidence is of concern, and other evidence for the compound should be evaluated for consistency with that finding.

Issue 34

Comment summary: Citing PAH as an example, commentors state that the documents have been inconsistent in qualitative determinations of carcinogenicity.

Response: In cases such as PAH where one criterion has to be set for an entire class of compounds, the Agency does not state that each chemical in the class is a carcinogen, as implied by the commentor. Therefore, the PAH example cited by the commentor does not show that the Agency is inconsistent in classifying compounds as carcinogenic.

The intended interpretation of the criterion is that the risk is less than 10^{-5} whenever the total concentration of all PAH compounds in water is less than the criterion. In a hypothetical case where all of the PAH compounds in a sample are non-carcinogenic, the criterion would be too strict; however, this situation seldom occurs. In most cases where PAH is detected, a mixture of compounds occurs and in calculating the criterion the assumption is made that all components have the same carcinogenic potency as benzo-a-pyrene.

Issue 35

Comment summary: Bis(2-chloroisopropyl)ether (BCIE) yielded negative results in an NCI bioassay. Nonetheless, the cancer based criteria based on an upper limit of the true response rate was calculated because of the structural similarity of BCIE to other carcinogenic chloroalkyl ethers. The commentor states that this is inappropriate.

Response: As a response to the public comments, the Agency has changed its interpretation of data on bis(2-chloroisopropyl)ether (BCIE). It is no longer considered to be carcinogenic and, therefore, a criterion based on carcinogenic data is not calculated.

Issue 36

Comment summary: Using the criteria for chromium and asbestos as examples, the commentors state that data on inhalation carcinogenicity should not be used to derive criteria if oral carcinogenicity tests are negative.

Response: The criteria for chromium (Cr) was derived on a marginally significant digestive cancer incidence which occurred from inhalation exposure (Enterline epidemiology study). The digestive system cancer is assumed to be caused by chromium (Cr) which is removed from the respiratory system by mucociliary action and then swallowed. This is comparable to exposure to chromium in drinking water. Cr (VI) has not been adequately tested for its carcinogenic potential in animals; therefore, further studies to assess the carcinogenicity of Cr (VI) by the oral route would be desirable and necessary before it is concluded that oral tests are negative.

Asbestos has been shown to cause peritoneal mesothelioma in humans and is also associated with a significant increase in human gastrointestinal cancers. These are caused by inhaled asbestos. Since up to 99 percent of the inhaled asbestos is eventually swallowed, the Agency feels that asbestos-contaminated water could cause the same type of gastrointestinal cancers as inhaled asbestos.

H. Joint Action/Cocarcinogenicity

Issue 37

Comment summary: The commentors emphasized the potential importance of cocarcinogenicity and possible synergistic effects among carcinogens.

Response: The potential importance of cocarcinogenicity and possible synergistic effects among carcinogens has not been addressed by the CAG in deriving water quality criteria, since sufficient data is not available at this time to make decisive judgments related to these issues.

I. Site Specific vs. Total Tumors

Issue 38

Comment summary: No public comments specifically addressed this issue. However, the methodology committee should discuss the appropriateness of using data on total tumors for quantitative risk assessment.

Response: Since chemicals generally exert their carcinogenic effects at specific organ sites, the incidence of tumors at the responding sites is the most relevant information to consider in making either qualitative or quantitative evaluations of hazard. The instances where the tumor incidence at all sites combined is elevated, but no one site or group of sites is significantly increased, are regarded as weak evidence of carcinogenicity.

J. General Issues

Issue 39

Comment summary: Single unverified bioassays should not be used for establishing criteria for dichlorobenzene.

Response: The comment does not refer to carcinogenicity data since no carcinogenic information was available on dichlorobenzene.

Issue 40

Comment summary: Some comments expressed concern with the types of studies used to derive criteria. Another comment implies that only data published in referenced journals should be used. Two commentors recommend that explicit reasons be developed for accepting or rejecting studies.

Response: The evaluations of bioassay studies for carcinogenicity by the CAG is sufficiently detailed to be equivalent to that given in peer reviewed journals.

Issue 41

Comment summary: The EPA "has used animal studies without adequately considering the nature of the toxic agent and its mechanism of action, the conditions of exposure, or the physiological characteristics of the test organism."

Response: The Agency routinely considers all of the available toxicological data cited by the commentor and agrees that these factors are important.

Issue 42

Comment summary: Several comments questioned the appropriateness of using studies from one route of exposure—particularly inhalation—to establish criteria for ingestion.

Response: If a given chemical induced a carcinogenic effect by inhalation at a distant site, it is likely that the compound could also produce a carcinogenic effect by other routes of administration. Therefore, the Agency considers it appropriate to use inhalation data to derive criteria for ingestion, recognizing the difficulty of determining the dose.

Issue 43

Comment summary: Treating all of the proposed criteria as if they were based upon equally valid data is not scientifically sound: EPA must make explicit the nature, extent, and quality of the data utilized to estimate criteria.

Response: The Agency has indicated which criteria should be regarded as

marginal based on the nature of the available data.

Issue 44

Comment summary: Criteria based on carcinogenic effects might not be adquate to protect humans from mutagenic, teratogenic, or other toxic effects.

Response: The U.S. EPA Office of Health and Environmental Assessment is currently developing guidelines for estimating the human risk to substances producing mutagenic, teratogenic, and reproductive effects.

Appendix

I. An Improved Procedure for Deriving Water Quality Criteria

As discussed in the methodology document (1981)* the Carcinogen Assessment Group (CAG) has adopted a new prodedure which is more systematic than the one-hit procedure used previously by the CAG for calculating the water quality criteria. The model selected for the low dose extrapolation is given by

$$P(d)=1-\exp[-(q_0+q_1d+\ \ldots\ +q_kd^k)]$$

At low doses, the upper confidence limit for the extra risk

$$A(d) = \frac{P(d) - P(o)}{1 - P(o)}$$

has the form

$$A_U(d) = 1-\exp\ (-q_1^*d) \simeq q_1^*\ d.$$

That is, the risk $A_u(d)$ is always linerarly related to d at low doses. The constant q_1^* corresponding to the 95 percent upper confidence limit for A(d) is taken as the carcinogenic potency for calculating the water quality criteria.

Instead of extrapolating with the one-hit model based on the lowest dose group showing statistically significant response as previously used by the CAG, the new procedure is employed because of the following reasons: (1) the procedure is more systematic; (2) it invokes fewer arbitrary assumptions; (3) the assumption of the low-dose linearity is not essential in the use of the model, and; (4) it incorporates data from all of the dose groups which are consistent with the multistage model. At the same time, it is conceptually consistent with the linear non-threshold concept on which the one-hit procedure was based.

The Agency recognizes that there is no really solid scientific basis for any mathematical extrapolation model which relates carcinogen exposure to cancer risks at the extremely low level of concentration that must be dealt with in evaluating the environmental hazards. For practical reasons such low levels of risk cannot be measured directly either by animal experiments or by epidemiologic studies. We must, therefore, depend on our current understanding of the mechanisms of carcinogenesis for guidance as to which risk model to use. At the present time the dominat view of the carcinogenic process involves the concept that most agents that cause cancer also cause irreversible damage to DNA. This position is reflected by the fact that a very large proportion of agents that cause cancer are also mutagenic.

There is reason to expect the quantal type of biological response that is characteristic of mutagenesis is associated with a linear non-threshold dose-response relationship. Indeed, there is substantial evidence from mutagenesis studies with both ionizing radiation and a wide variety of chemicals that this type of dose-response model is the appropriate one to use. This is particularly true at the lower end of the dose-response curve; at higher doses, there can be an upward curvature probably reflecting non-threshold dose-response relationships. The linear non-threshold model is also consistent with the relatively few epidemiological studies of cancer responses to specific agents that contain enough information to make the evaluation possible (e.g., radiation induced leukemia, breast and thyroid cancer, and skin cancer induced by arsenic in drinking water, and liver cancer, induced by aflatoxin in the diet). There is also some evidence from animal experiments that is consistent with the linear non-threshold model (e.g., liver tumors induced in mice by 2-acetylaminofluorene in the large scale ED_{01} study at the National Center of Toxicological Research and the initiation stage of the two-stage carcinogenesis model in the rat liver and the mouse skin).

Because it has the best, albeit limited, scientific basis of any of the current mathematical extrapolation models, the linear non-threshold model has been adopted as the primary basis for risk extrapolation to low levels of the dose-relationship. The risk estimates made with this model should be regarded as conservative, representing the most plausible upper limit for risk, i.e., the true risk is not likely to be higher than the estimate but it could be smaller.

II. Comparison of the new Procedure with the Old (One-Hit) Procedure

The Agency had previously calculated the slope b based on the one-hit model $P=1-\exp-bd$, using only the data from the lowest dose group where the incidence rate is statistically significantly different from the control group (see Federal Register, Part V, Thursday, March 15, 1979). The point estimate b was taken as the carcinogenic potency for the compound. Unlike the new procedure, the upper confidence limit was not used because the CAG recognized that the one-hit model is usually conservative at low doses and thus the point estimate b of the slope was considered as an upper limit of the true carcinogenic potency. This ad hoc approach was used because it is simple and easy to understand.

Since b was considered an upper limit in an ad hoc sense, it would be interesting to compare the new procedure with the one-hit procedure by calculating the ratio of two carcinogenic potencies b/q_1^* for 21 chemical compounds in the Proposed Water Quality Criteria Documents which have data from at least three dose groups. Except for chlordane and heptachlor the new procedure agrees with the one-hit procedure within a factor of 2. When the one-hit procedure is modified (Table 1) the two procedures become comparable. Therefore, the old procedure could be used as a simple and quick way of estimating the carcinogenic potency.

Table 1.—*Ratio of Carcinogenic Potencies*

Chemicals	b/q_1^*	
Chlordane	3.33	[1] (0.83)
Heptachlor	2.50	[1] (0.78)
Carbon tetrachloride	1.47	
PAH	1.35	
HCB	1.19	
1,2-Dichloroethane	1.18	
Acrylonitrile	1.10	
Hexachloroethane	1.06	
2,4,6-Trichlorophenol	.98	
Trichloroethylene	.95	
Hexachlorobutadiene	.88	
Chloroform	.81	
1,1,2,2-Tetrachloroethane	.75	
1,1,2-Trichloroethane	.70	
TCDD	.65	
2,4-Dinitrotoluene	.63	
Vinyl chloride	.63	
Toxaphene	.56	
Aldrin	.56	
Bis(chloromethyl)ether	.53	
Hydrazobenzene	.50	

[1] The parenthesized value is the ratio b/q_1^* when b is calculated based on the 95 percent upper confidence limit (one-sided) for the incidence rate in the next lowest dose group, instead of using the incidence rate of the lowest dose group showing statistically significantly different from the control group. This modification was recommended when the tumorigenic responses exhibit sharp upward curvature with low doses.

[FR Doc. 80-36186 Filed 11-26-80; 8:45 am]

BILLING CODE 6560-29-M

* Carcinogen Assessment Group's Procedure for Calculating Water Quality Criteria. Updated 1981.