System with whole body of fish or invertebrates:

a. For each trophic level, a species mean measured baseline BAF shall be calculated as the geometric mean if more than one measured BAF is available for a given species.

b. For each trophic level, the geometric mean of the species mean measured baseline BAFs shall be used as the wildlife BAF for that chemical.

3. If an acceptable measured baseline BAF is not available for an inorganic chemical and one or more acceptable whole-body laboratory-measured BCFs are available for the chemical, a predicted baseline BAF shall be calculated by multiplying the geometric mean of the BCFs times a FCM. The FCM will be 1.0 unless chemical-specific biomagnification data support using a multiplier other than 1.0. The predicted baseline BAF shall be used as the wildlife BAF for that chemical.

VIII. Final Review

For both organic and inorganic chemicals, human health and wildlife BAFs for both trophic levels shall be reviewed for consistency with all available data concerning the bioaccumulation, bioconcentration, and metabolism of the chemical. For example, information concerning octanol-water partitioning, molecular size, or other physicochemical properties that might enhance or inhibit bioaccumulation should be considered for organic chemicals. BAFs derived in accordance with this methodology should be modified if changes are justified by available data.

IX. Literature Cited

ASTM. 1990. Standard Practice for Conducting Bioconcentration Tests with Fishes and Saltwater Bivalve Molluscs. Standard E 1022. American Society for Testing and Materials, Philadelphia, PA.

TABLE B–1—FOOD-CHAIN MULTIPLIERS FOR TROPHIC LEVELS 2, 3 & 4

Log K_{OW}	Trophic level 2	Trophic[1] level 3	Trophic level 4
2.0	1.000	1.005	1.000
2.5	1.000	1.010	1.002
3.0	1.000	1.028	1.007
3.1	1.000	1.034	1.007
3.2	1.000	1.042	1.009
3.3	1.000	1.053	1.012
3.4	1.000	1.067	1.014
3.5	1.000	1.083	1.019
3.6	1.000	1.103	1.023
3.7	1.000	1.128	1.033
3.8	1.000	1.161	1.042
3.9	1.000	1.202	1.054
4.0	1.000	1.253	1.072
4.1	1.000	1.315	1.096
4.2	1.000	1.380	1.130
4.3	1.000	1.491	1.178

TABLE B–1—FOOD-CHAIN MULTIPLIERS FOR TROPHIC LEVELS 2, 3 & 4—Continued

Log K_{OW}	Trophic level 2	Trophic[1] level 3	Trophic level 4
4.4	1.000	1.614	1.242
4.5	1.000	1.766	1.334
4.6	1.000	1.950	1.459
4.7	1.000	2.175	1.633
4.8	1.000	2.452	1.871
4.9	1.000	2.780	2.193
5.0	1.000	3.181	2.612
5.1	1.000	3.643	3.162
5.2	1.000	4.188	3.873
5.3	1.000	4.803	4.742
5.4	1.000	5.502	5.821
5.5	1.000	6.266	7.079
5.6	1.000	7.096	8.551
5.7	1.000	7.962	10.209
5.8	1.000	8.841	12.050
5.9	1.000	9.716	13.964
6.0	1.000	10.556	15.996
6.1	1.000	11.337	17.783
6.2	1.000	12.064	19.907
6.3	1.000	12.691	21.677
6.4	1.000	13.228	23.281
6.5	1.000	13.662	24.604
6.6	1.000	13.980	25.645
6.7	1.000	14.223	26.363
6.8	1.000	14.355	26.669
6.9	1.000	14.388	26.669
7.0	1.000	14.305	26.242
7.1	1.000	14.142	25.468
7.2	1.000	13.852	24.322
7.3	1.000	13.474	22.856
7.4	1.000	12.987	21.038
7.5	1.000	12.517	18.967
7.6	1.000	11.708	16.749
7.7	1.000	10.914	14.388
7.8	1.000	10.069	12.050
7.9	1.000	9.162	9.840
8.0	1.000	8.222	7.798
8.1	1.000	7.278	6.012
8.2	1.000	6.361	4.519
8.3	1.000	5.489	3.311
8.4	1.000	4.683	2.371
8.5	1.000	3.949	1.663
8.6	1.000	3.296	1.146
8.7	1.000	2.732	0.778
8.8	1.000	2.246	0.521
8.9	1.000	1.837	0.345
9.0	1.000	1.493	0.226

[1] The FCMs for trophic level 3 are the geometric mean of the FCMs for sculpin and alewife.

APPENDIX C TO PART 132—GREAT LAKES WATER QUALITY INITIATIVE METHODOLOGIES FOR DEVELOPMENT OF HUMAN HEALTH CRITERIA AND VALUES

Great Lakes States and Tribes shall adopt provisions consistent with (as protective as) this appendix.

I. INTRODUCTION

Great Lakes States and Tribes shall adopt provisions consistent with this appendix C to ensure protection of human health.

A. *Goal*. The goal of the human health criteria for the Great Lakes System is the protection of humans from unacceptable exposure to toxicants via consumption of contaminated fish and drinking water and from ingesting water as a result of participation in water-oriented recreational activities.

B. *Definitions*.

Acceptable daily exposure (ADE). An estimate of the maximum daily dose of a substance which is not expected to result in adverse noncancer effects to the general human population, including sensitive subgroups.

Adverse effect. Any deleterious effect to organisms due to exposure to a substance. This includes effects which are or may become debilitating, harmful or toxic to the normal functions of the organism, but does not include non-harmful effects such as tissue discoloration alone or the induction of enzymes involved in the metabolism of the substance.

Carcinogen. A substance which causes an increased incidence of benign or malignant neoplasms, or substantially decreases the time to develop neoplasms, in animals or humans. The classification of carcinogens is discussed in section II.A of appendix C to part 132.

Human cancer criterion (HCC). A Human Cancer Value (HCV) for a pollutant that meets the minimum data requirements for Tier I specified in appendix C.

Human cancer value (HCV). The maximum ambient water concentration of a substance at which a lifetime of exposure from either: drinking the water, consuming fish from the water, and water-related recreation activities; or consuming fish from the water, and water-related recreation activities, will represent a plausible upper-bound risk of contracting cancer of one in 100,000 using the exposure assumptions specified in the Methodologies for the Development of Human Health Criteria and Values in appendix C of this part.

Human noncancer criterion (HNC). A Human Noncancer Value (HNV) for a pollutant that meets the minimum data requirements for Tier I specified in appendix C of this part.

Human noncancer value (HNV). The maximum ambient water concentration of a substance at which adverse noncancer effects are not likely to occur in the human population from lifetime exposure via either: drinking the water, consuming fish from the water, and water-related recreation activities; or consuming fish from the water, and water-related recreation activities using the Methodologies for the Development of Human Health criteria and Values in appendix C of this part.

Linearized multi-stage model. A conservative mathematical model for cancer risk assessment. This model fits linear dose-response curves to low doses. It is consistent with a no-threshold model of carcinogenesis, i.e., exposure to even a very small amount of the substance is assumed to produce a finite increased risk of cancer.

Lowest observed adverse effect level (LOAEL). The lowest tested dose or concentration of a substance which resulted in an observed adverse effect in exposed test organisms when all higher doses or concentrations resulted in the same or more severe effects.

No observed adverse effect level (NOAEL). The highest tested dose or concentration of a substance which resulted in no observed adverse effect in exposed test organisms where higher doses or concentrations resulted in an adverse effect.

Quantitative structure activity relationship (OSAR) or structure activity relationship (SAR). A mathematical relationship between a property (activity) of a chemical and a number of descriptors of the chemical. These descriptors are chemical or physical characteristics obtained experimentally or predicted from the structure of the chemical.

Relative source contribution (RSC). The factor (percentage) used in calculating an HNV or HNC to account for all sources of exposure to a contaminant. The RSC reflects the percent of total exposure which can be attributed to surface water through water intake and fish consumption.

Risk associated dose (RAD). A dose of a known or presumed carcinogenic substance in (mg/kg/day) which, over a lifetime of exposure, is estimated to be associated with a plausible upper bound incremental cancer risk equal to one in 100,000.

Slope factor. Also known as q_1*, slope factor is the incremental rate of cancer development calculated through use of a linearized multistage model or other appropriate model. It is expressed in (mg/kg/day) of exposure to the chemical in question.

Threshold effect. An effect of a substance for which there is a theoretical or empirically established dose or concentration below which the effect does not occur.

Uncertainty factor (UF). One of several numeric factors used in operationally deriving criteria from experimental data to account for the quality or quantity of the available data.

C. *Level of Protection*. The criteria developed shall provide a level of protection likely to be without appreciable risk of carcinogenic and/or noncarcinogenic effects. Criteria are a function of the level of designated risk or no adverse effect estimation, selection of data and exposure assumptions. Ambient criteria for single carcinogens shall not be set at a level representing a lifetime upper-bound incremental risk greater than one in 100,000 of developing cancer using the hazard assessment techniques and exposure assumptions described herein. Criteria affording protection from noncarcinogenic effects shall be established at levels that, taking into account uncertainties, are considered likely to be without an appreciable risk

of adverse human health effects (i.e., acute, subchronic and chronic toxicity including reproductive and developmental effects) during a lifetime of exposure, using the risk assessment techniques and exposure assumptions described herein.

D. *Two-tiered Classification*. Chemical concentration levels in surface water protective of human health shall be derived based on either a Tier I or Tier II classification. The two Tiers are primarily distinguished by the amount of toxicity data available for deriving the concentration levels and the quantity and quality of data on bioaccumulation.

II. MINIMUM DATA REQUIREMENTS

The best available toxicity data on the adverse health effects of a chemical and the best data on bioaccumulation factors shall be used when developing human health Tier I criteria or Tier II values. The best available toxicity data shall include data from well-conducted epidemiologic and/or animal studies which provide, in the case of carcinogens, an adequate weight of evidence of potential human carcinogenicity and, in the case of noncarcinogens, a dose-response relationship involving critical effects biologically relevant to humans. Such information should be obtained from the EPA Integrated Risk Information System (IRIS) database, the scientific literature, and other informational databases, studies and/or reports containing adverse health effects data of adequate quality for use in this procedure. Strong consideration shall be given to the most currently available guidance provided by IRIS in deriving criteria or values, supplemented with any recent data not incorporated into IRIS. When deviations from IRIS are anticipated or considered necessary, it is strongly recommended that such actions be communicated to the EPA Reference Dose (RfD) and/or the Cancer Risk Assessment Verification Endeavor (CRAVE) workgroup immediately. The best available bioaccumulation data shall include data from field studies and well-conducted laboratory studies.

A. *Carcinogens*. Tier I criteria and Tier II values shall be derived using the methodologies described in section III.A of this appendix when there is adequate evidence of potential human carcinogenic effects for a chemical. It is strongly recommended that the EPA classification system for chemical carcinogens, which is described in the 1986 EPA Guidelines for Carcinogenic Risk Assessment (U.S. EPA, 1986), or future modifications thereto, be used in determining whether adequate evidence of potential carcinogenic effects exists. Carcinogens are classified, depending on the weight of evidence, as either human carcinogens, probable human carcinogens, or possible human carcinogens. The human evidence is considered inadequate and therefore the chemical cannot be classified as a human carcinogen, if one of two conditions exists: (a) there are few pertinent data, or (b) the available studies, while showing evidence of association, do not exclude chance, bias, or confounding and therefore a casual interpretation is not credible. The animal evidence is considered inadequate, and therefore the chemical cannot be classified as a probable or possible human carcinogen, when, because of major qualitative or quantitative limitations, the evidence cannot be interpreted as showing either the presence or absence of a carcinogenic effect.

Chemicals are described as ''human carcinogens'' when there is sufficient evidence from epidemiological studies to support a causal association between exposure to the chemicals and cancer. Chemicals described as ''probable human carcinogens'' include chemicals for which the weight of evidence of human carcinogenicity based on epidemiological studies is limited. Limited human evidence is that which indicates that a causal interpretation is credible, but that alternative explanations, such as chance, bias, or confounding, cannot adequately be excluded. Probable human carcinogens are also agents for which there is sufficient evidence from animal studies and for which there is inadequate evidence or no data from epidemiologic studies. Sufficient animal evidence is data which indicates that there is an increased incidence of malignant tumors or combined malignant and benign tumors: (a) in multiple species or strains; (b) in multiple experiments (e.g., with different routes of administration or using different dose levels); or (c) to an unusual degree in a single experiment with regard to high incidence, unusual site or type of tumor, or early age at onset. Additional evidence may be provided by data on dose-response effects, as well as information from short-term tests (such as mutagenicity/genotoxicity tests which help determine whether the chemical interacts directly with DNA) or on chemical structure, metabolism or mode of action.

''Possible human carcinogens'' are chemicals with limited evidence of carcinogenicity in animals in the absence of human data. Limited animal evidence is defined as data which suggests a carcinogenic effect but are limited because: (a) The studies involve a single species, strain, or experiment and do not meet criteria for sufficient evidence (see preceding paragraph); or (b) the experiments are restricted by inadequate dosage levels, inadequate duration of exposure to the agent, inadequate period of follow-up, poor survival, too few animals, or inadequate reporting; or (c) the studies indicate an increase in the incidence of benign tumors only. More specifically, this group can include a wide variety of evidence, e.g., (a) a malignant tumor response in a single well-

conducted experiment that does not meet conditions for sufficient evidence, (b) tumor response of marginal statistical significance in studies having inadequate design or reporting, (c) benign but not malignant tumors with an agent showing no response in a variety of short-term tests for mutagenicity, and (d) response of marginal statistical significance in a tissue known to have a high or variable background rate.

1. *Tier I:* Weight of evidence of potential human carcinogenic effects sufficient to derive a Tier I HCC shall generally include human carcinogens, probable human carcinogens and can include, on a case-by-case basis, possible human carcinogens if studies have been well-conducted albeit based on limited evidence, when compared to studies used in classifying human and probable human carcinogens. The decision to use data on a possible human carcinogen for deriving Tier I criteria shall be a case-by-case determination. In determining whether to derive a Tier I HCC, additional evidence that shall be considered includes but is not limited to available information on mode of action, such as mutagenicity/genotoxicity (determinations of whether the chemical interacts directly with DNA), structure activity, and metabolism.

2. *Tier II:* Weight of evidence of possible human carcinogenic effects sufficient to derive a Tier II human cancer value shall include those possible human carcinogens for which there are at a minimum, data sufficient for quantitative risk assessment, but for which data are inadequate for Tier I criterion development due to a tumor response of marginal statistical significance or inability to derive a strong dose-response relationship. In determining whether to derive Tier II human cancer values, additional evidence that shall be considered includes but is not limited to available information on mode of action such as mutagenicity/genotoxicity (determinations of whether the chemical interacts directly with DNA), structure activity and metabolism. As with the use of data on possible human carcinogens in developing Tier I criteria, the decision to use data on possible human carcinogens to derive Tier II values shall be made on a case-by-case basis.

B. *Noncarcinogens.* All available toxicity data shall be evaluated considering the full range of possible health effects of a chemical, i.e., acute/subacute, chronic/subchronic and reproductive/developmental effects, in order to best describe the dose-response relationship of the chemical, and to calculate human noncancer criteria and values which will protect against the most sensitive endpoint(s) of toxicity. Although it is desirable to have an extensive database which considers a wide range of possible adverse effects, this type of data exists for a very limited number of chemicals. For many others, there is a range in quality and quantity of data available. To assure minimum reliability of criteria and values, it is necessary to establish a minimum database with which to develop Tier I criteria or Tier II values. The following represent the minimum data sets necessary for this procedure.

1. *Tier I:* The minimum data set sufficient to derive a Tier I human HNC shall include at least one well-conducted epidemiologic study or animal study. A well-conducted epidemiologic study for a Tier I HNC must quantify exposure level(s) and demonstrate positive association between exposure to a chemical and adverse effect(s) in humans. A well-conducted study in animals must demonstrate a dose response relationship involving one or more critical effect(s) biologically relevant to humans. (For example, study results from an animal whose pharmacokinetics and toxicokinetics match those of a human would be considered most biologically relevant.) Ideally, the duration of a study should span multiple generations of exposed test species or at least a major portion of the lifespan of one generation. This type of data is currently very limited. By the use of uncertainty adjustments, shorter term studies (such as 90-day subchronic studies) with evaluation of more limited effect(s) may be used to extrapolate to longer exposures or to account for a variety of adverse effects. For Tier I criteria developed pursuant to this procedure, such a limited study must be conducted for at least 90 days in rodents or 10 percent of the lifespan of other appropriate test species and demonstrate a no observable adverse effect level (NOAEL). Chronic studies of one year or longer in rodents or 50 percent of the lifespan or greater in other appropriate test species that demonstrate a lowest observable adverse effect level (LOAEL) may be sufficient for use in Tier I criterion derivation if the effects observed at the LOAEL were relatively mild and reversible as compared to effects at higher doses. This does not preclude the use of a LOAEL from a study (of chronic duration) with only one or two doses if the effects observed appear minimal when compared to effect levels observed at higher doses in other studies.

2. *Tier II:* When the minimum data for deriving Tier I criteria are not available to meet the Tier I data requirements, a more limited database may be considered for deriving Tier II values. As with Tier I criteria, all available data shall be considered and ideally should address a range of adverse health effects with exposure over a substantial portion of the lifespan (or multiple generations) of the test species. When such data are lacking it may be necessary to rely on less extensive data in order to establish a Tier II value. With the use of appropriate uncertainty factors to account for a less extensive database, the minimum data sufficient

to derive a Tier II value shall include a NOAEL from at least one well-conducted short-term repeated dose study. This study shall be of at least 28 days duration, in animals demonstrating a dose-response, and involving effects biologically relevant to humans. Data from studies of longer duration (greater than 28 days) and LOAELs from such studies (greater than 28 days) may be more appropriate in some cases for derivation of Tier II values. Use of a LOAEL should be based on consideration of the following information: severity of effect, quality of the study and duration of the study.

C. *Bioaccumulation factors (BAFs).*

1. *Tier I for Carcinogens and Noncarcinogens:* To be considered a Tier I cancer or noncancer human health criterion, along with satisfying the minimum toxicity data requirements of sections II.A.1 and II.B.1 of this appendix, a chemical must have the following minimum bioaccumulation data. For all organic chemicals either: (a) a field-measured BAF; (b) a BAF derived using the BSAF methodology; or (c) a chemical with a BAF less than 125 regardless of how the BAF was derived. For all inorganic chemicals, including organometals such as mercury, either: (a) a field-measured BAF or (b) a laboratory-measured BCF.

2. *Tier II for Carcinogens and Noncarcinogens:* A chemical is considered a Tier II cancer or noncancer human health value if it does not meet either the minimum toxicity data requirements of sections II.A.1 and II.B.1 of this appendix or the minimum bioaccumulation data requirements of section II.C.1 of this appendix.

III. Principles for Development of Tier I Criteria or Tier II Values

The fundamental components of the procedure to calculate Tier I criteria or Tier II values are the same. However, certain of the aspects of the procedure designed to account for short-duration studies or other limitations in data are more likely to be relevant in deriving Tier II values than Tier I criteria.

A. *Carcinogens.*

1. A non-threshold mechanism of carcinogenesis shall be assumed unless biological data adequately demonstrate the existence of a threshold on a chemical-specific basis.

2. All appropriate human epidemiologic data and animal cancer bioassay data shall be considered. Data specific to an environmentally appropriate route of exposure shall be used. Oral exposure should be used preferentially over dermal and inhalation since, in most cases, the exposure routes of greatest concern are fish consumption and drinking water/incidental ingestion. The risk associated dose shall be set at a level corresponding to an incremental cancer risk of one in 100,000. If acceptable human epidemiologic data are available for a chemical, it shall be used to derive the risk associated dose. If acceptable human epidemiologic data are not available, the risk associated dose shall be derived from available animal bioassay data. Data from a species that is considered most biologically relevant to humans (i.e., responds most like humans) is preferred where all other considerations regarding quality of data are equal. In the absence of data to distinguish the most relevant species, data from the most sensitive species tested, i.e., the species showing a carcinogenic effect at the lowest administered dose, shall generally be used.

3. When animal bioassay data are used and a non-threshold mechanism of carcinogenicity is assumed, the data are fitted to a linearized multistage computer model (e.g., Global '86 or equivalent model). Global '86 is the linearized multistage model, derived by Howe, Crump and Van Landingham (1986), which EPA uses to determine cancer potencies. The upper-bound 95 percent confidence limit on risk (or, the lower 95 percent confidence limit on dose) at the one in 100,000 risk level shall be used to calculate a risk associated dose (RAD). Other models, including modifications or variations of the linear multistage model which are more appropriate to the available data may be used where scientifically justified.

4. If the duration of the study is significantly less than the natural lifespan of the test animal, the slope may be adjusted on a case-by-case basis to compensate for latent tumors which were not expressed (e.g., U.S. EPA, 1980) In the absence of alternative approaches which compensate for study durations significantly less than lifetime, the permitting authority may use the process described in the 1980 National Guidelines (see 45 FR 79352).

5. A species scaling factor shall be used to account for differences between test species and humans. It shall be assumed that milligrams per surface area per day is an equivalent dose between species (U.S. EPA, 1986). All doses presented in mg/kg bodyweight will be converted to an equivalent surface area dose by raising the mg/kg dose to the 2/3 power. However, if adequate pharmacokinetic and metabolism studies are available, these data may be factored into the adjustment for species differences on a case-by-case basis.

6. Additional data selection and adjustment decisions must also be made in the process of quantifying risk. Consideration must be given to tumor selection for modeling, e.g., pooling estimates for multiple tumor types and identifying and combining benign and malignant tumors. All doses shall be adjusted to give an average daily dose over the study duration. Adjustments in the rate of tumor response must be made for

early mortality in test species. The goodness-of-fit of the model to the data must also be assessed.

7. When a linear, non-threshold dose response relationship is assumed, the RAD shall be calculated using the following equation:

$$RAD = \frac{0.00001}{q_1^*}$$

Where:

RAD=risk associated dose in milligrams of toxicant per kilogram body weight per day (mg/kg/day).

0.00001 (1×10^{-5})=incremental risk of developing cancer equal to one in 100,000.

q_1^*=slope factor $(mg/kg/day)^{-1}$.

8. If human epidemiologic data and/or other biological data (animal) indicate that a chemical causes cancer via a threshold mechanism, the risk associated dose may, on a case-by-case basis, be calculated using a method which assumes a threshold mechanism is operative.

B. *Noncarcinogens.*

1. Noncarcinogens shall generally be assumed to have a threshold dose or concentration below which no adverse effects should be observed. Therefore, the Tier I criterion or Tier II value is the maximum water concentration of a substance at or below which a lifetime exposure from drinking the water, consuming fish caught in the water, and ingesting water as a result of participating in water-related recreation activities is likely to be without appreciable risk of deleterious effects.

For some noncarcinogens, there may not be a threshold dose below which no adverse effects should be observed. Chemicals acting as genotoxic teratogens and germline mutagens are thought to possibly produce reproductive and/or developmental effects via a genetically linked mechanism which may have no threshold. Other chemicals also may not demonstrate a threshold. Criteria for these types of chemicals will be established on a case-by-case basis using appropriate assumptions reflecting the likelihood that no threshold exists.

2. All appropriate human and animal toxicologic data shall be reviewed and evaluated. To the maximum extent possible, data most specific to the environmentally relevant route of exposure shall be used. Oral exposure data should be used preferentially over dermal and inhalation since, in most cases, the exposure routes of greatest concern are fish consumption and drinking water/incidental ingestion. When acceptable human data are not available (e.g., well-conducted epidemiologic studies), animal data from species most biologically relevant to humans shall be used. In the absence of data to distinguish the most relevant species, data from the most sensitive animal species tested, i.e., the species showing a toxic effect at the lowest administered dose (given a relevant route of exposure), should generally be used.

3. Minimum data requirements are specified in section II.B of this appendix. The experimental exposure level representing the highest level tested at which no adverse effects were demonstrated (NOAEL) from studies satisfying the provisions of section II.B of this appendix shall be used for criteria calculations. In the absence of a NOAEL, the LOAEL from studies satisfying the provisions of section II.B of this appendix may be used if it is based on relatively mild and reversible effects.

4. Uncertainty factors shall be used to account for the uncertainties in predicting acceptable dose levels for the general human population based upon experimental animal data or limited human data.

a. An uncertainty factor of 10 shall generally be used when extrapolating from valid experimental results from studies on prolonged exposure to average healthy humans. This 10-fold factor is used to protect sensitive members of the human population.

b. An uncertainty factor of 100 shall generally be used when extrapolating from valid results of long-term studies on experimental animals when results of studies of human exposure are not available or are inadequate. In comparison to a, above, this represents an additional 10-fold uncertainty factor in extrapolating data from the average animal to the average human.

c. An uncertainty factor of up to 1000 shall generally be used when extrapolating from animal studies for which the exposure duration is less than chronic, but greater than subchronic (e.g., 90 days or more in length), or when other significant deficiencies in study quality are present, and when useful long-term human data are not available. In comparison to b, above, this represents an additional UF of up to 10-fold for less than chronic, but greater than subchronic, studies.

d. An UF of up to 3000 shall generally be used when extrapolating from animal studies for which the exposure duration is less than subchronic (e.g., 28 days). In comparison to b above, this represents an additional UF of up to 30-fold for less than subchronic studies (e.g., 28-day). The level of additional uncertainty applied for less than chronic exposures depends on the duration of the study used relative to the lifetime of the experimental animal.

e. An additional UF of between one and ten may be used when deriving a criterion from a LOAEL. This UF accounts for the lack of an identifiable NOAEL. The level of additional uncertainty applied may depend upon the severity and the incidence of the observed adverse effect.

f. An additional UF of between one and ten may be applied when there are limited effects data or incomplete sub-acute or chronic toxicity data (e.g., reproductive/developmental data). The level of quality and quantity of the experimental data available as well as structure-activity relationships may be used to determine the factor selected.

g. When deriving an UF in developing a Tier I criterion or Tier II value, the total uncertainty, as calculated following the guidance of sections 4.a through f, cited above, shall not exceed 10,000 for Tier I criteria and 30,000 for Tier II values.

5. All study results shall be converted, as necessary, to the standard unit for acceptable daily exposure of milligrams of toxicant per kilogram of body weight per day (mg/kg/day). Doses shall be adjusted for continuous exposure (i.e., seven days/week, 24 hours/day, etc.).

C. *Criteria and Value Derivation.*

1. *Standard Exposure Assumptions.* The following represent the standard exposure assumptions used to calculate Tier I criteria and Tier II values for carcinogens and noncarcinogens. Higher levels of exposure may be assumed by States and Tribes pursuant to Clean Water Act (CWA) section 510, or where appropriate in deriving site-specific criteria pursuant to procedure 1 in appendix F to part 132.

BW = body weight of an average human (BW = 70kg).

WC_d = per capita water consumption (both drinking and incidental exposure) for surface waters classified as public water supplies = two liters/day.

—or—

WC_r = per capita incidental daily water ingestion for surface waters not used as human drinking water sources = 0.01 liters/day.

FC = per capita daily consumption of regionally caught freshwater fish = 0.015kg/day (0.0036 kg/day for trophic level 3 and 0.0114 kg/day for trophic level 4).

BAF = bioaccumulation factor for trophic level 3 and trophic level 4, as derived using the BAF methodology in appendix B to part 132.

2. *Carcinogens.* The Tier I human cancer criteria or Tier II values shall be calculated as follows:

$$HCV = \frac{RAD \times BW}{WC + \left[\left(FC_{TL3} \times BAF_{TL3}^{HH}\right) + \left(FC_{TL4} \times BAF_{TL4}^{HH}\right)\right]}$$

Where:

HCV=Human Cancer Value in milligrams per liter (mg/L).

RAD=Risk associated dose in milligrams toxicant per kilogram body weight per day (mg/kg/day) that is associated with a lifetime incremental cancer risk equal to one in 100,000.

BW=weight of an average human (BW=70 kg).

WC_d=per capita water consumption (both drinking and incidental exposure) for surface waters classified as public water supplies=two liters/day.

or

WC_r=per capita incidental daily water ingestion for surface waters not used as human drinking water sources=0.01 liters/day.

FC_{TL3}=mean consumption of trophic level 3 of regionally caught freshwater fish=0.0036 kg/day.

FC_{TL4}=mean consumption of trophic level 4 of regionally caught freshwater fish=0.0114 kg/day.

BAF^{HH}_{TL3}=bioaccumulation factor for trophic level 3 fish, as derived using the BAF methodology in appendix B to part 132.

BAF^{HH}_{TL4}=bioaccumulation factor for trophic level 4 fish, as derived using the BAF methodology in appendix B to part 132.

3. *Noncarcinogens.* The Tier I human noncancer criteria or Tier II values shall be calculated as follows:

$$HNV = \frac{ADE \times BW \times RSC}{WC + \left[\left(FC_{TL3} \times BAF_{TL3}^{HH}\right) + \left(FC_{TL4} \times BAF_{TL4}^{HH}\right)\right]}$$

Where:

HNV=Human noncancer value in milligrams per liter (mg/L).

ADE=Acceptable daily exposure in milligrams toxicant per kilogram body weight per day (mg/kg/day).

RSC=Relative source contribution factor of 0.8. An RSC derived from actual exposure data may be developed using the methodology outlined by the 1980 National Guidelines (see 45 FR 79354).

BW=weight of an average human (BW=70 kg).

WC_d=per capita water consumption (both drinking and incidental exposure) for surface waters classified as public water supplies=two liters/day.

or

WC_r=per capita incidental daily water ingestion for surface waters not used as human drinking water sources=0.01 liters/day.

FC_{TL3}=mean consumption of trophic level 3 fish by regional sport fishers of regionally caught freshwater fish=0.0036 kg/day.

FC_{TL4}=mean consumption of trophic level 4 fish by regional sport fishers of regionally caught freshwater fish=0.0114 kg/day.

$BAF^{HH}{}_{TL3}$=human health bioaccumulation factor for edible portion of trophic level 3 fish, as derived using the BAF methodology in appendix B to part 132.

$BAF^{HH}{}_{TL4}$=human health bioaccumulation factor for edible portion of trophic level 4 fish, as derived using the BAF methodology in appendix B to part 132.

IV. References

A. Howe, R.B., K.S. Crump and C. Van Landingham. 1986. Computer Program to Extrapolate Quantitative Animal Toxicity Data to Low Doses. Prepared for EPA under subcontract #2–251U–2745 to Research Triangle Institute.

B. U.S. Environmental Protection Agency. 1980. Water Quality Criteria Availability, Appendix C Guidelines and Methodology Used in the Preparation of Health Effects Assessment Chapters of the Consent Decree Water Quality Criteria Documents. Available from U.S. Environmental Protection Agency, Office of Water Resource Center (WH–550A), 1200 Pennsylvania Ave., NW., Washington, DC 20460.

C. U.S. Environmental Protection Agency. 1986. Guidelines for Carcinogen Risk Assessment. Available from U.S. Environmental Protection Agency, Office of Water Resource Center (WH–550A), 1200 Pennsylvania Ave., NW., Washington, DC 20460.

Appendix D to Part 132—Great Lakes Water Quality Initiative Methodology for the Development of Wildlife Criteria

Great Lakes States and Tribes shall adopt provisions consistent with (as protective as) this appendix.

I. Introduction

A. A Great Lakes Water Quality Wildlife Criterion (GLWC) is the concentration of a substance which is likely to, if not exceeded, protect avian and mammalian wildlife populations inhabiting the Great Lakes basin from adverse effects resulting from the ingestion of water and aquatic prey taken from surface waters of the Great Lakes System. These criteria are based on existing toxicological studies of the substance of concern and quantitative information about the exposure of wildlife species to the substance (i.e., food and water consumption rates). Since toxicological and exposure data for individual wildlife species are limited, a GLWC is derived using a methodology similar to that used to derive noncancer human health criteria (Barnes and Dourson, 1988; NAS, 1977; NAS, 1980; U.S. EPA, 1980). Separate avian and mammalian values are developed using taxonomic class-specific toxicity data and exposure data for five representative Great Lakes basin wildlife species. The wildlife species selected are representative of avian and mammalian species resident in the Great Lakes basin which are likely to experience the highest exposures to bioaccumulative contaminants through the aquatic food web; they are the bald eagle, herring gull, belted kingfisher, mink, and river otter.

B. This appendix establishes a methodology which is required when developing Tier I wildlife criteria for bioaccumulative chemicals of concern (BCCs). The use of the equation provided in the methodology is encouraged, but not required, for the development of Tier I criteria or Tier II values for pollutants other than those identified in Table 6–A for which Tier I criteria or Tier II values are determined to be necessary for the protection of wildlife in the Great Lakes basin. A discussion of the methodology for deriving Tier II values can be found in the Great Lakes Water Quality Initiative Technical Support Document for Wildlife Criteria (Wildlife TSD).

C. In the event that this methodology is used to develop criteria for pollutants other than BCCs, or in the event that the Tier II methodology described in the Wildlife TSD is used to derive Tier II values, the methodology for deriving bioaccumulation factors under appendix B to part 132 must be used in either derivation. For chemicals which do not biomagnify to the extent of BCCs, it may be appropriate to select different representative species which are better examples of species with the highest exposures for the given chemical. The equation presented in this methodology, however, is still encouraged. In addition, procedure 1 of appendix F of this part describes the procedures for calculating site-specific wildlife criteria.

D. The term ''wildlife value'' (WV) is used to denote the value for each representative species which results from using the equation presented below, the value obtained from averaging species values within a class, or any value derived from application of the site-specific procedure provided in procedure