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Fish Consumption Advisories: Toward a Unified, Scientifically Credible Approach[1]

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A model is proposed for fish consumption advisories based on consensus-derived risk assessment values for common contaminants in fish and the latest risk assessment methods. The model accounts in part for the expected toxicity to mixtures of chemicals, the underlying uncertainties in the health and exposure data, and the amount of contaminated fish consumed. Application of the model to a larger number of chemicals is possible. Noncancer toxicity is used as an example, but this model is applicable for risks from cancer as well. A second related model is proposed that is useful for comparing potential risks among sites (e.g., rivers and lakes).

INTRODUCTION

State and Federal health scientists and administrators have grappled for years with the outwardly simple problem of developing a framework for setting consumption advisories for contaminated fish. The efforts toward such a framework appear justified since humans represent one of the ultimate receptors for aquatic contaminants (e.g., Humphrey, 1987) and public concern over fish consumption is evident in the popular press (e.g., Snyder, 1988). Unfortunately, this apparently simple problem is particularly difficult because its resolution must account for different contaminant levels in different fish species, widely divergent measured concentrations of a given contaminant over a diverse ecosystem, widely varying fish preparation and eating habits, different mixtures of chemicals in the same fish with different toxic properties, and uncertainties inherent in the exposure and health components of the advisory. Moreover, several well-wrought but different positions and advisories exist, including states (e.g., Minnesota Department of Public Health, 1986; Michigan Department of

[1] This paper has been through the required scientific review of the Office of Research and Development, but the views expressed here do not necessarily reflect the views or policies of the Environmental Protection Agency.

Public Health, 1989; Wisconsin Division of Health, 1989), Federal organizations [e.g., U.S. Food and Drug Administration (Scheuplein, 1988), the U.S. Environmental Protection Agency (U.S. EPA, 1989), Interagency EPA/FDA Standing Committee, 1988], and an international agreement (International Joint Commission, 1978). Despite these difficulties, the resolution of this problem is foremost among scientists and managers in various agencies, and novel suggestions for this problem's resolution have been made (Minnesota Department of Public Health, 1986; Clark *et al.,* 1987; Olson and Anderson, 1988). A comprehensive methodology for assessing hazards of contaminants in seafood has been proposed as well (Brown *et al.,* 1988).

The purpose of this paper is to evaluate current fish consumption advisories of the Great Lakes and to conduct a mixtures risk assessment using noncancer toxicity of selected chemicals. The resulting evaluation and assessment (which is useful for assessing carcinogenic risks as well) provides a sound scientific model for developing credible fish consumption advisories in general. A second model is proposed, based in large part on U.S. EPA, 1989, that is flexible and easy to use on a site-specific basis, and allows ranking of different sites as to potential risk.

METHODS

The following discussion of fish consumption advisories and related agency positions is not necessarily meant to be comprehensive, but reflects the thinking on these issues as related to the Great Lakes of the United States. Estimates of fish contamination are given in many papers. Three have been selected here (Clark *et al.,* 1987; DeVault *et al.,* 1986; DeVault, 1985) in part because they relate to the Great Lakes, but more importantly because they give relatively good fish contamination data with either standard deviations or 95% confidence levels for a number of chemicals.

Definitions used throughout this paper are consistent with the parlance of the U.S. EPA (1990). These definitions are meant for illustration only, other terms are used in different organizations and countries. These definitions include:

Critical effect—The first adverse effect, or its known precursor, that occurs as the dose rate increases.

Fish intake—The amount of fish (in kg/day) calculated from Eq. 1 that is based on multiplying a chemical-specific, or chemical mixtures RfD or RSD (in mg of chemical/kg of body weight/day) by an assumed body weight (in kg), and dividing the result by a measured amount of contaminant(s) in fish flesh (in mg of chemical per kg of fish).

Lowest-observed-adverse-effect level (LOAEL)—The lowest exposure level at which there are statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control group.

Modifying factor (MF)—An uncertainty factor that is greater than zero and less than or equal to 10; the magnitude of the MF depends upon the professional assessment of scientific uncertainties of the study and data base not explicitly treated with the standard uncertainty factors (i.e., the number of animals tested); the default value for the MF is 1. The use of MF is explained more fully in Barnes and Dourson (1988).

No-observed-adverse-effect level (NOAEL)—An exposure level at which there are no statistically or biologically significant increases in the frequency or severity of adverse effects between the exposed population and its appropriate control; *some effects may be produced at this level, but they are considered neither adverse nor precursors to specific adverse effects.* In an experiment with several NOAELs, the regulatory focus is primarily on the highest one, leading to the common usage of the term NOAEL as the highest exposure without adverse effect.

Reference dose (RfD)—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.

Risk specific dose (RSD)—The dose of a chemical (in mg/kg/day) that is associated with a specified upper limit of excess lifetime cancer risk. The usual interpretation of an RSD is that the excess cancer risk is unlikely to exceed the stated value, but it could be lower.

Uncertainty factor—One of several, generally 10-fold factors, used in operationally deriving the reference dose (RfD) from experimental data. UFs are intended to account for (1) the variation in sensitivity among the members of the human population; (2) the uncertainty in extrapolating animal data to the case of humans; (3) the uncertainty in extrapolating from data obtained in a study that is of less-than-lifetime exposure; (4) the uncertainty in using LOAEL data rather than NOAEL data; and (5) the inability of any single study to adequately address all possible adverse outcomes in man.

Table 1 gives a list of chemicals detected in Lake Michigan fish with their corresponding critical effect, NOAEL and LOAEL, uncertainty factor and modifying factor, RfD, confidence levels in the RfD, and associated criteria. Toxicity data are from the U.S. EPA's Integrated Risk Information System (IRIS) (U.S. EPA 1990). This system contains over 400 concensus-derived risk values on chemicals of interest in environmental pollution. (Please note that the values listed in Table 1 may have changed since the preparation of this manuscript, and are for illustrative purposes only. Definitive values with their associated caveats should be obtained on-line from IRIS.) Recent U.S. EPA guidelines on chemical mixtures (U.S. EPA, 1986) and on the consumption of contaminated fish and shellfish (U.S. EPA, 1989) give details on technical issues only briefly described here. The reader is referred to these more comprehensive texts for additional information.

RESULTS

Existing Efforts

Table 2 summarizes the fish consumption advisories or related efforts of various agencies and the method proposed here as to whether five major technical issues have been addressed:

1. the different contaminant levels among species and locations,
2. varying fish preparation (e.g., skin on or skin off fillets, fat removal), and fish-eating habits (e.g., number and sizes of meals consumed),
3. the number of contaminants,
4. the mixture of contaminants within a given species, and

TABLE 1

NTEREST IN LAKE MICHIGAN FISH AND THEIR CORRESPONDING CRITICAL EFFECTS, NOAELS AND LOAELS, UFS AND MFS, REFERENCE D
(RFDS), CONFIDENCES IN THE RFD AND RESULTING CRITERIA BASED ON STANDARD EXPOSURE ASSUMPTIONS[a]

	CAS number	Critical effect	NOAEL/LOAEL (mg/kg/day)	UF×MF	RfD (mg/kg/day)	Confidence in the RfD	Crite (mg/kg
	309-00-2	Liver toxicity	None, 0.025	1,000×1	3E−5	Medium	1E
	117-81-7	Increased liver weight	None, 19	1,000×1	2E−2	Medium	7E
	57-74-9	Liver necrosis	None, 0.045	1,000×1	5E−5	Medium	2E
	1861-32-1	Increased kidney weight	50, 500	100×1	5E−1	Medium	2E
	50-29-3	Liver lesions	0.05, 0.25	100×1	5E−4	Medium	2E
	60-57-1	Liver lesions	0.005, 0.05	100×1	5E−5	Medium	2E
	84-66-2	Several	750, 3160	1,000×1	8E−1	Low	3E
	84-74-2	Increased mortality	125, 600	1,000×1	1E−1	Low	4E
	115-29-7	Kidney toxicity	None, 0.15	3,000×1	5E−5	Medium	2E
	76-44-8	Liver weight increase	0.15, 0.25	300×1	5E−4	Low	1E
	1024-57-3	Liver weight increase	None, 0.0125	1,000×1	1.3E−5	Low	5E
	118-74-1	Liver toxicity	0.08, 0.29	100×1	8E−4	Medium	3E
ıe	87-68-3	Kidney toxicity	0.2, 2	100×1	2E−3	Low	7E
ıexane	58-89-9	Liver and kidney toxicity	0.33, 1.55	1,000×1	3E−4	Medium	1E
	67-72-1	Kidney toxicity	1, 15	1,000×1	1E−3	Medium	4E
	22967-92-6	CNS effects	None, 0.003	10×1	3E−4	Medium	1E
	2385-85-5	Decreased pup survival	None, 0.015	10,000×1	2E−6	Low	7E
:	608-93-5	Liver and kidney toxicity	None, 8.3	1,000×1	8E−4	Low	3E
	87-86-5	Liver and kidney pathology	3, 10	100×1	3E−2	Medium	1E
henyls	12674-11-2	Reproductive and liver effects	0.01, 0.1	100×1	1E−4	NR[c]	4E
	100-42-5	Blood and liver effects	200, 400	1,000×1	2E−1	Medium	7E
	95-94-3	Kidney lesions	0.34, 3.4	1,000×1	3E−4	Low	1E
	1582-09-8	Increased proteins in urine	None, 2.5	1,000×1	3E−3	Medium	1E

ıation: IRIS (U.S. EPA, 1990) for all values except polychlorinated biphenyls (PCBs). This latter value is estimated in existing EPA documents
[S are updated on a monthly basis; thus the information in this table may be out of date. Please check IRIS or call IRIS User Support (513/56
n.
= (RfD (mg/kg bw/day) × 70 kg bw)/(0.02 kg of fish/day). For example, if the RfD was 0.002 mg/kg/day (i.e., 2E−3) the criterion (roundec
; of chemical/kg of fish (i.e., 7 ppm); that is, 0.002 mg of chemical/kg of body weight/day (RfD) × 70 kg of body weight (assumed) ÷ 0.02 kg
mption) = 7 mg of chemical/kg of fish. Exceeding this criterion does not categorically result in adverse effects, in part because exceeding the R
sult in adverse effects (see text for discussion).
l; value not on IRIS.

TABLE 2

FISH CONSUMPTION ADVISORIES OR RELATED EFFORTS IN RELATIONSHIP TO WHETHER OR NOT SELECTED TECHNICAL ISSUES HAVE BEEN EXPLICITLY ADDRESSED

Fish consumption advisory (or related effort)	Technical issues[a]: Extent of contamination	Fish preparation and eating	Number of chemicals	Mixtures of chemicals	Underlying uncertainties
Clark *et al.*, 1987	Yes	Limited	Few	Yes	Limited
Dourson and Clark (this paper)	Yes	Limited	Many	Yes	Limited
Michigan DPH, 1989	Yes	Yes	Few	No	No
Minnesota DPH, 1986	Yes	Yes	Few	No	No
Olson and Anderson, 1988	Yes	Limited	Few	No	No
Scheuplein, 1988	No	Limited	Few	No	No
Wisconsin DH, 1989	Yes	Limited	Few	No	No
U.S. EPA, 1989	Yes	Yes	Many	Yes	Limited

[a] See text for explanation.

5. the uncertainty inherent in the exposure and health components of the advisory.

Nearly all established fish consumption advisories have accounted for the different contaminant levels among the species and locations, and many have given advice on safer fish preparation habits, such as fat removal (Wisconsin Department of Health and Social Services, 1989; Michigan Department of Public Health, 1989; Minnesota Department of Public Health, 1986). Fish preparation can affect the level of contaminants in edible portions (e.g., Cichy *et al.*, 1979). State fish consumption advisories, however, have often been silent on the question of how much contaminated fish can be eaten and whether eating fish of several species is safe, although the topic generally has been extensively discussed by state officials. A notable exception to this general rule is the previously employed advisory by the Minnesota Department of Public Health (1986). This previous advisory classified the population into long- and short-term consumers and guided consumers on the selection of the number of meals from different classes of contaminated fish.

Most fish consumption advisories surveyed have depended on U.S. FDA action levels for selected contaminants in commercial fish. For example, the fish advisories of Michigan and Wisconsin recommend no consumption of any fish when 50% or more have contamination above a pesticide or PCB action level (MDPH, 1989; WDH, 1989). If 10 to 50% of the fish are contaminated above an action level, the advisory recomments that women and children not consume these fish. Adult males are to "limit" consumption of these fish. If 10% or less of fish are contaminated above an action level, no specific advice on the amount of fish which should be consumed is provided. (Until recently an exception to this reliance on action levels has been the

Minnesota Department of Public Health, 1986, which has developed advisories on the basis of a more definitive risk assessment.) While such action levels are essential on a national basis to regulate the sale of fish among states (Scheuplein, 1988), such levels may not be appropriate as a basis for site (or situation)-specific risk assessment for at least six reasons:

1. they only address a limited number of chemicals (U.S. EPA, 1989),
2. they do not clearly articulate the underlying fish consumption estimates,
3. they incorporate risk management considerations, such as commercial sale of fish, which may not be appropriate in some local situations (U.S. EPA, 1989),
4. they cannot be used quantitatively to estimate the potential health risk from mixtures of chemicals commonly found in fish,
5. they do not account for uncertainties inherent in the action level's underlying health and exposure values, and
6. they are set higher than known contamination levels of many pesticides and PCBs according to recent surveys (U.S. FDA, 1990).

Not surprisingly, the development of comprehensive advisories has proved difficult. However, unified, multidisciplinary efforts in setting fish consumption advisories now exist in several state agencies. Several comprehensive risk assessment approaches have been published (U.S. EPA, 1986, 1989; Brown *et al.,* 1988). Moreover, a coordinated fish-monitoring program has been established (Interagency Co-operative Agreement, 1985). Thus, a framework exists for the development of a more scientifically credible model in estimating fish consumption advisories.

In addition, the U.S. FDA and the U.S. EPA created a joint standing committee in regard to chemical residues in fish and shellfish (Interagency EPA/FDA, 1988). The purpose of this committee is to guide the policy of these two federal agencies in an area where both have obligations and mutual interests. One of the policies of this committee is to encourage the development of site-specific guidance. For example, this policy allows regional federal offices and state agencies to propose fish consumption advisories using information particular to a given site (e.g., the type of contamination and species affected), and exposure assumption particular to a given population (e.g., the average fish consumption of people living in Cincinnati versus those living in Chicago).

The Proposed Fish Consumption Advisory

We propose developing fish consumption advisories on the basis of a species and site-specific mixtures risk assessment. The advisories would be developed in two steps. The first would be to calculate a daily fish intake (i.e., kg of fish per day) from the appropriate RfDs for noncancer toxicity or risk specific doses (RDSs) for cancer in units of milligrams of chemical per kilogram of body weight per day, multiplied by an assumed body weight (bw) (in our example 70 kg is used to illustrate the concept), and divided by the measured (or estimated) levels of contaminants in skin-on fish fillets in units of milligrams of chemical per kilogram of fish (i.e., ppm). That is:

$$\text{fish intake (kg of fish/day)} = \frac{\text{RfD (mg of chemical/kg bw/day)} \times 70 \text{ (kg bw)}}{\text{fish concentration (mg of chemical/kg of fish)}}. \quad (1)$$

Mixtures of chemicals in fish flesh that cause both noncancer and cancer toxicity

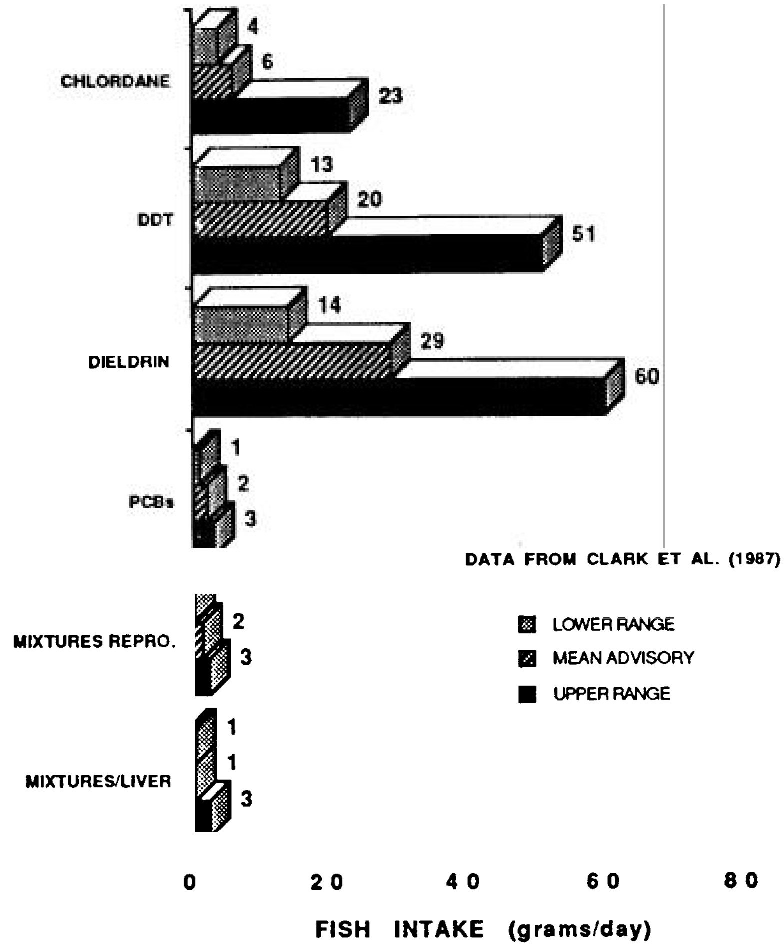

FIG. 1. Calculated fish intakes (from Eq. 1) for individual chemicals and their expected mixture in Lake Michigan lake trout of >25 in. Values for PCBs are based upon the RFD for aroclor 1016; higher chlorinated PCBs may yield lower intakes.

would necessitate the calculation of separate fish intakes, since current theoretical methods do not exist to combine both risks (U.S. EPA, 1986).

Figure 1 shows fish intakes derived for lake trout > 25 inches for single chemicals by the equation above, and using RfDs as provided in Table 1 and exposure data from Clark *et al.* (1987). Different bars for each chemical are based on the means and upper and lower ranges (based on standard deviations) for exposure data of Clark *et al.* (1987). Individual mean fish intakes are as low as 2 g of fish/day (i.e., 0.002 kg) for PCBs (using the RfD for Aroclor 1016, similar to Aroclor 1242) to as high as 29 g/day for dieldin. A mixtures risk assessment was also conducted as specified in the appendix and indicates a range in the fish intakes between 1 and 3 g/day with a mean value of 1 g for the liver and 2 g for reproductive effects. Table 3 shows similar data for lake trout of 20–25 and <20 inches in size. A mixtures risk assessment (for the liver) on these smaller trout shows a range of fish intake between 2 and 4 g/day with a mean value of about 3 g for 20–25-inch fish, and a mean value of 7 g/day for <20-inch fish.

Figure 2 shows a similar analysis for the Black River using the data of DeVault (1985). Based on individual chemicals, fish intakes vary from a low of 5 grams per day for PCBs to over 300 g per day for many chemicals. A mixtures risk assessment

TABLE 3

CALCULATED FISH INTAKES IN GRAMS/DAY FOR MEDIUM AND SMALL LAKE TROUT FROM LAKE MICHIGAN[a]

Chemical	Trout 20–25 in			Trout < 20 in		
	Lower SD[b]	Mean	Upper SD	Lower SD	Mean	Upper SD
Chlordane		10	18	—	35	
DDT		4			117	—
Dieldrin		4			175	—
PCBs[d]				7	10	17
Mixtures/liver		3	4	—	7	—
Mixtures/reproductive	3	4	6	—	10	—

[a] Data from Clark *et al.* (1987). Values for large lake trout (i.e., >25 in) can be found in Fig. 1. Values for trout < 20 inches were extrapolated, in part, from larger trout.

[b] SD, standard deviation.

[c] Information not available.

[d] PCB values are based upon the reference dose for Aroclor 1016. Lower RfDs might be estimated for other more chlorinated PCBs. These lower values would be associated with lower calculated fish intakes.

on these data yield a value of about 5 g of fish per day. (Only single values of chemical concentration were available in this paper; thus, no range in the fish intake is presented.)

In both of these figures the calculated fish intake is inversely proportional to the chemical contamination in fish—more highly contaminated fish yield lower fish intakes. In contrast, calculated fish intakes are directly proportional to the RfD or RSD. For example, if a lower RfD for higher chlorinated PCBs was used in the above equation, then the calculated fish intakes would also be proportionally lower.

The second step in the development of the proposed fish consumption advisories is to estimate the amount of fish consumed per meal. For example, an approximate twofold difference exists in the sizes of individual fish meals, that is $\frac{1}{4}$ lb (about 110 g) to $\frac{1}{2}$ lb (about 230 g) (U.S. EPA 1988a). Fortuitously, the combination of this range of meal size and the frequency of fish meals eaten over a given period of time roughly follows a logarithmic scale. Thus, the consumption of 3 to 10 g/of fish per day is in the range of eating one $\frac{1}{4}$- to $\frac{1}{2}$-lb fish meal per month; the consumption of 10 to 30 g/day is in the range of eating one $\frac{1}{4}$- to $\frac{1}{2}$-lb meal per week; the consumption of 30 to 100 g/day is in the range of eating three $\frac{1}{4}$- to $\frac{1}{2}$-lb meals per week; the consumption of 100 to 300 g/day is in the range of eating one $\frac{1}{4}$- to $\frac{1}{2}$-lb meal per day.

The proposed fish consumption advisory follows directly from a comparison of calculated fish intake and the estimated amount of fish consumed per meal and meal frequency. For example, compare the calculated fish intakes (Fig. 1 and Table 3) with the amount of fish consumed (Table 4). The calculated fish intake for the largest Lake Michigan lake trout (Fig. 1) of 1 g/day is less than the consumption of one meal per month and, therefore, may lead to a potentially do-not-eat public advisory based on noncancer toxicity alone. For either smaller size trout (Table 3), a calculated fish intake of 3 or 7 g/day is associated with the expected fish consumption of one meal per month for noncancer toxicity alone.

In comparison, current fish consumption advisories on Lake Michigan lake trout for the states of Michigan (MDPH, 1989) and Wisconsin (WDH, 1989) recommend

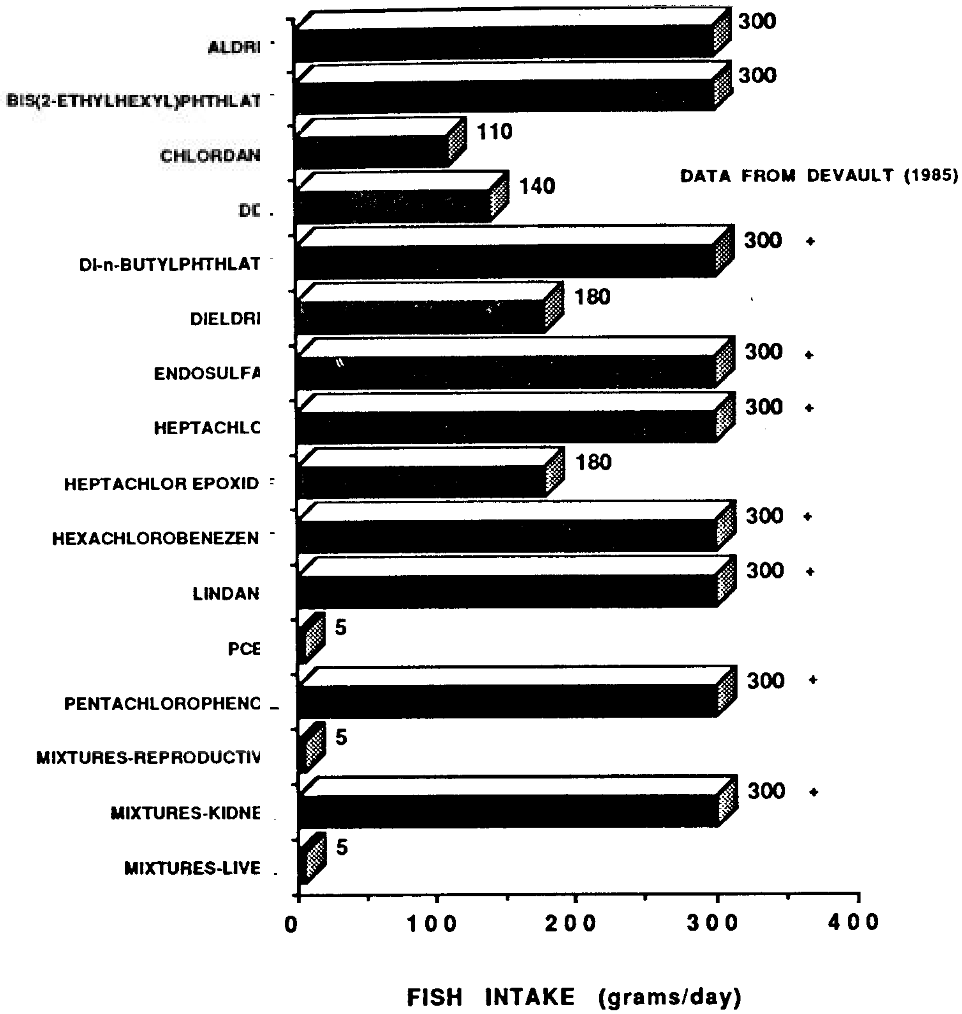

FIG. 2. Calculated fish intakes (from Eq. 1) on individual chemicals and their expected mixture in Black River fish.

no consumption of the lake trout > 23 in. Lake trout of 20–23 in. are not to be eaten by women or children, and adult males are advised not to eat more than one meal per week. No specific consumption advice is provided for lake trout of <20 in.

As discussed in Clark *et al.* (1987) a fish consumption advisory would also need to consider cancer risks. For example, at a rate of one meal a month over a lifetime, the

TABLE 4

RELATIONSHIP OF THE PROPOSED FISH CONSUMPTION ADVISORY TO THE CALCULATED FISH INTAKE

Fish consumption advisory (fish meal of $\frac{1}{4}$ to $\frac{1}{2}$ lb assumed)	Calculated fish intake (g of fish per day, from Eq. (1))
Do not eat	nil to 3
One meal a month	>3 to 10
One meal a week	>10 to 30
Three meals a week	>30 to 100
One meal a day	>100 to 300
Unlimited consumption	>300

upper limit cancer risks for consumption of the medium size lake trout (20 to 25 in.) would be approximately one in 10,000 from the contamination by PCBs, DDT, dieldrin, chlordane, and metabolites of these compounds. Thus, selecting an upper limit cancer risk level of one in 10,000 would necessitate a consumption rate less than one meal per month.

Criteria Development

Criteria are estimates of chemical concentrations in an environmental medium (e.g., fish flesh) that are associated with a specified lifetime cancer risk or without appreciable noncancer health risk. Criteria are appropriately developed without risk management considerations. The criteria in Table 1 have been estimated using an RfD, a fish consumption of 0.02 kg/day, and an assumed body weight (bw) of 70 kg:

Criterion or acceptable level (AL) in mg of chemical per kg of fish)

$$\frac{\text{RfD (mg of chemical/kg bw/day)} \times 70 \text{ kg bw}}{0.02 \text{ kg of fish/day}}. \quad (2)$$

The assumption of about 0.02 kg (i.e., 20 g) of fish consumed per day (USDA, 1985) serves only to introduce the concept of criterion and show its practical applications. Other exposure and body weight assumptions could be used in the overall determination of criteria and may be more appropriate at a given site. This assumption of 20 g of fish per day falls in the range of eating one meal per week of about $\frac{1}{4}$–$\frac{1}{2}$ lb and approximates an average consumption rate. Please note, however, that estimates of daily fish consumption vary widely, depending upon which survey or model is used. For example, a fish consumption assumption of 100 g/day represents the 90th greater percentile as determined by surveys (Finch, 1973). This assumption falls in the range of eating three meals per week of about $\frac{1}{2}$ lb, and its use would result in more conservative criteria. Extensive discussions on the amount of fish consumed per day have occurred (U.S. EPA 1988a). For a more detailed discussion of criteria derivation for contaminants in fish please refer to U.S. EPA (1989).

A number of simple and interesting analyses can be conducted using criteria. For example, Fig. 3 shows four concentration/criterion ratios, that is, ratios of chemical concentrations in fish to their respective criteria, for Lake Michigan lake trout caught off Saugatuck in 1982. These ratios are calculated from the measured fish concentrations of chlordane, DDT (total), dieldrin, and PCBs (total) as reported by DeVault *et al.* (1986), and the corresponding criteria for these chemicals found in Table 1. Different bars for individual chemicals as shown in Fig. 3 are based on the means and 95% upper and lower confidence limits of contaminant levels as stated by DeVault *et al.* (1986). For an average fish consumption rate of 20 g/day, mean concentration/criterion ratios vary from a low value of about 0.4 for oxychlordane to a high value of about 14 for PCBs. A mixtures risk assessment, conducted as specified in U.S. EPA (1986) (see also the Appendix), results in higher ratios, ranging for liver toxicity from about 15 to 19, with a mean of 16. (For a high fish consumption amount of 100 g/day, mean criterion ratios vary from a low value of about 2 for oxychlordane to a high value of about 80 for PCBs.)

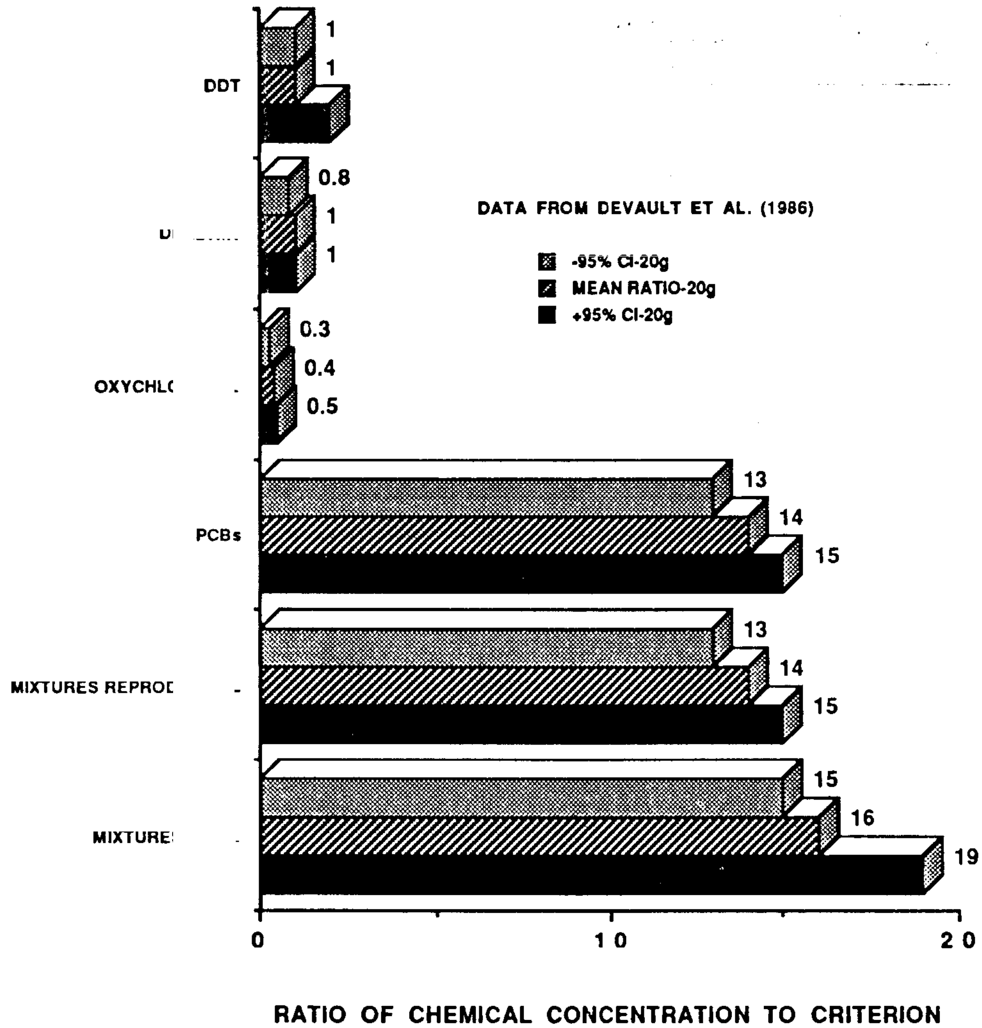

FIG. 3. Ratios of chemical concentration to criterion for individual chemicals and their expected mixture in Lake Michigan lake trout of unspecified size. Ratios > 1 indicate a potential hazard.

Ratios in excess of 1 may indicate potential hazards. For example, as the concentration/criterion ratio approaches 1 the concern for the potential hazard of the mixture and those consuming fish increases. As the ratios exceeds 1, the concern is the same as if the individual chemical exposure exceeded its acceptable level by the same proportion (U.S. EPA, 1986).

Another practical and easily applied use of criteria is in the comparison of contaminated fish from similar sites. For example, Figs. 4, 5, and 6 show concentration/criterion ratios for a number of chemicals from the Black, the Ashtabula, and the Sheboygan rivers, respectively. Ratios were calculated using the fish contamination data of DeVault (1985) and the corresponding criteria as found in Table 1. Using 20 g of fish per day, Fig. 4 shows a criterion ratio of 5 for liver toxicity from eating fish from the Black River after a noncancer mixtures risk assessment is performed. (Only single measurements of chemical contamination of fish were given for this site; thus no range exists for the criterion ratios. Furthermore, the DeVault (1985) study reported whole fish contaminant concentrations and not those in the edible portions. Thus, these data should only be used for comparison with other similarly derived data sets.) Figure 5 shows a value of about 6 to 32 for liver toxicity from eating fish in

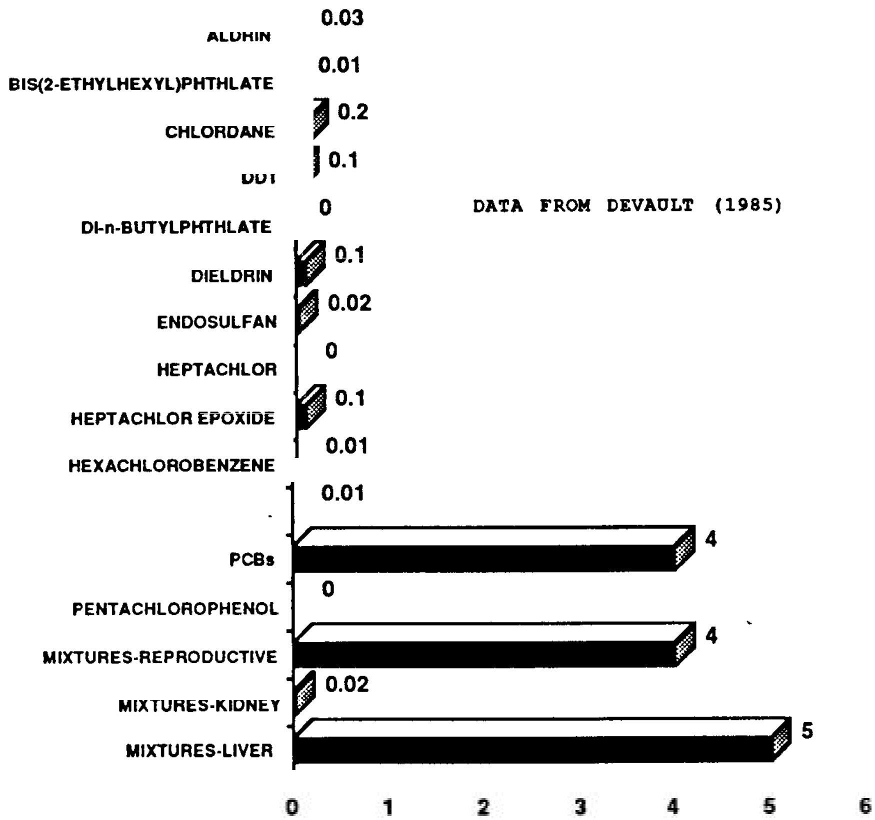

FIG. 4. Ratios of chemical concentration to criterion for individual chemicals and their expected mixture in Black River fish. Ratios > 1 indicate a potential hazard.

the Ashtabula River after a noncancer mixtures risk assessment is performed. Ranges indicate up to four measurements of fish chemical contamination for this site. Figure 6 shows a value of about ~120 to 300 for liver toxicity from eating fish in the Sheboygan River after a noncancer mixtures risk assessment is performed. Ranges in Fig. 6 indicate up to three measurements of chemical contamination in fish from this site.

Of obvious interest here is the ease with which such criteria analyses can handle a large number of chemicals found in fish flesh, making them ideal for use on a site-specific basis or in the evaluation of potential risk among sites.

DISCUSSION

The toxicity and exposure values listed in this paper are to only illustrate the proposed models. The U.S. EPA's IRIS (U.S. EPA, 1990) is a dynamic system whose values change depending on the latest toxicity data and/or evaluation. Likewise, environmental loadings of various contaminants discussed in this paper may have changed. A site-specific analysis using the local exposure data and current toxicity data (IRIS on-line, for example) is encouraged over the use of any chemical-specific information presented here.

Current fish consumption advisories can be improved through the use of the latest toxicity and exposure data on more than just a few chemicals and risk assessment

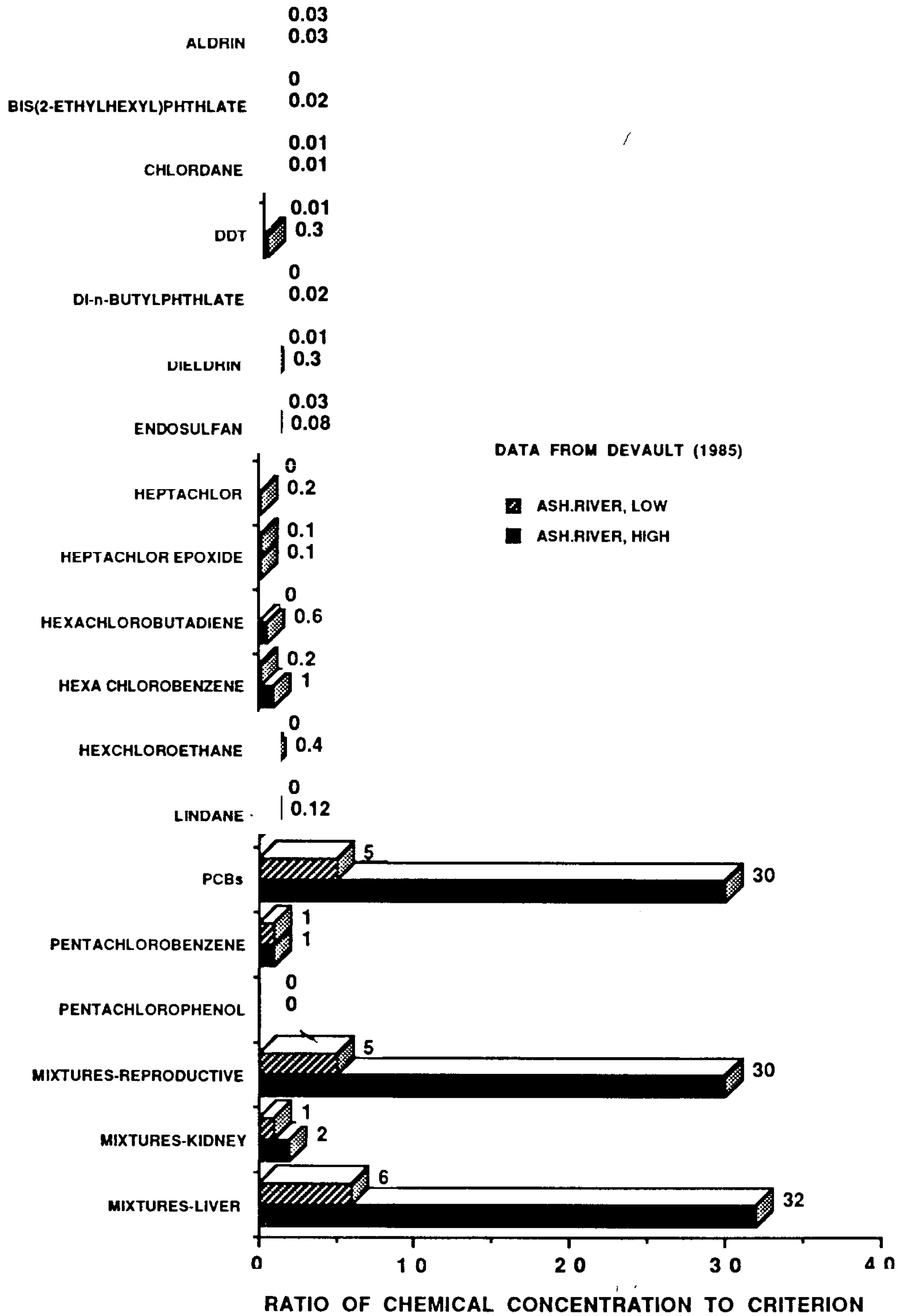

FIG. 5. Ratios of chemical concentration to criterion for individual chemicals and their expected mixture in Ashtabula River fish. Ratios > 1 indicate a potential hazard.

guidelines that have been widely reviewed and published (e.g., Brown *et al.,* 1988; U.S. EPA, 1986; 1989). The model for fish consumption advisories proposed in this paper (see Eq. 1, Figs. 1 and 2 and Tables 3 and 4) uses the health risk assessment values of numerous chemicals (U.S. EPA, 1990) in a framework that is supported by published guidelines for chemical mixtures and criterion development (U.S. EPA, 1986; 1989). Fish consumption advisories developed in this manner also correspond

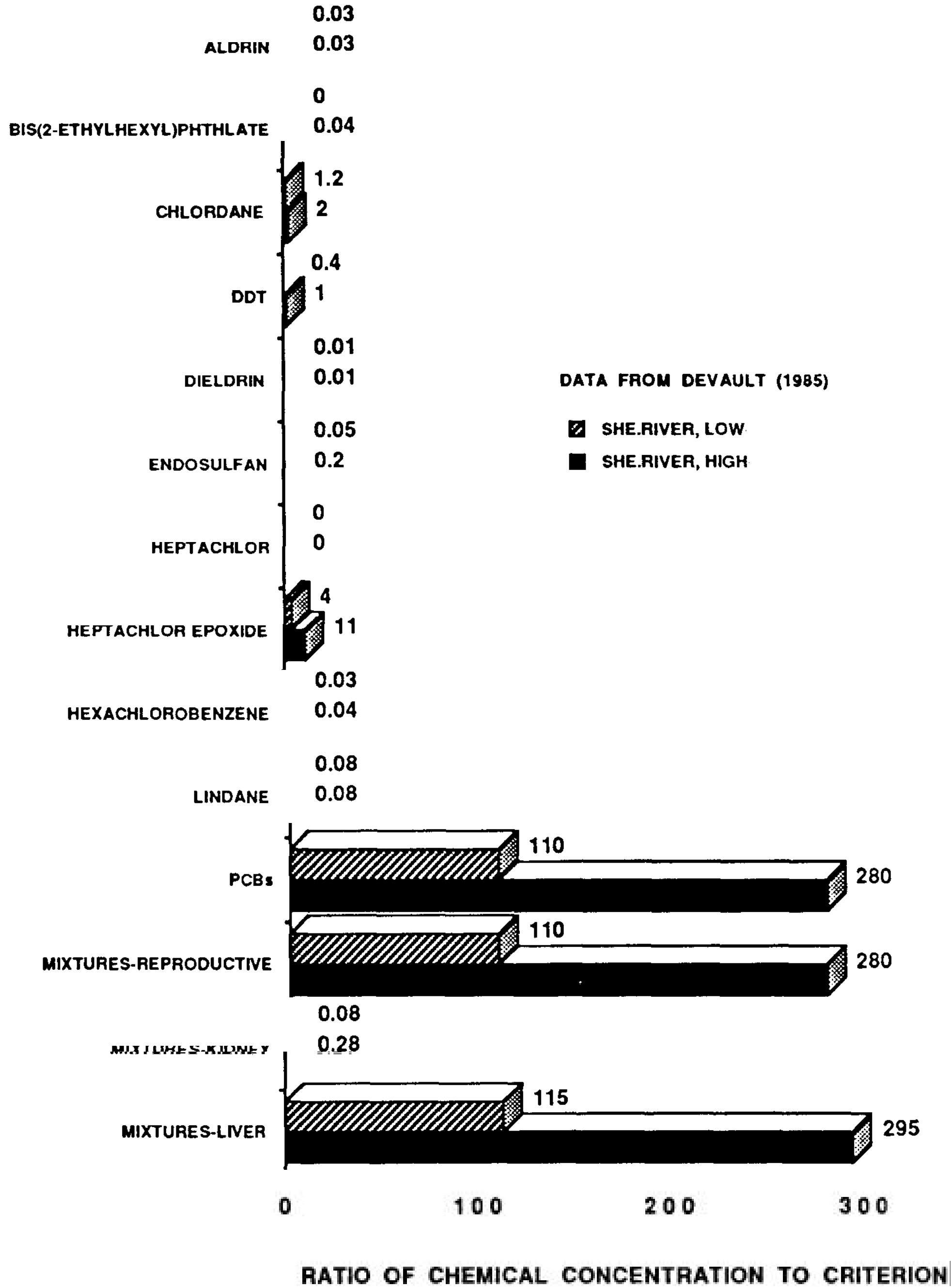

FIG. 6. Ratios of chemical concentration to criterion for individual chemicals and their expected mixture in Sheboygan River fish. Ratios > 1 indicate a potential hazard.

roughly with the variability in the underlying noncancer and cancer toxicity data [e.g., since RfDs are usually only precise to perhaps an order of magnitude (Barnes and Dourson, 1988)]. The proposed model also accounts for the amount of fish consumed by making fish consumption the dependent variable in Eq. 1. This model is also consistent with a basic tenet of the toxicologic sciences that the dose makes the poison (Klaassen *et al.,* 1986). To paraphrase this for fish consumption: the amount of contamination in fish is inversely related to the amount of fish that can be consumed. Equation 1 is a simple reflection of this basic principle.

Since theoretical methods to combine the health risks to mixtures of noncancer and cancer toxicities are not yet proposed (U.S. EPA, 1986), two scores may be necessary with this proposed model. However, U.S. EPA and state agencies often use upper limit lifetime cancer risks in the range of one in 10,000 to one in 1,000,000. Doses associated with these upper limit cancer risks might be used to estimate the amount of fish to be consumed, thus, offering a possible way to combine these two scores.

One potential difficulty with the proposed fish consumption advisory lies with the habit of infrequent fish consumption (i.e., once a month or once a week). Toxicologists seldom design studies with chemical exposures less frequent than once a day; subsequently, RfDs and RSDs are nearly always based on daily exposures (or exposures 5 days a week), and sometimes on nearly continuous chemical exposures. Thus, the use of RfDs and RSDs for infrequent fish consumption may underestimate the potential toxicity to humans, if this toxicity depends on a mechanism sensitive to large, intermittent doses. (This may occur more often with developmental toxic effects.) One potential solution to this technical problem would be to restrict public fish consumption advisories (see Table 4) to only three meals per week or more, thus, advising against consumption if the contamination resulted in the necessity of infrequent fish meals (i.e., only once a week or once a month).

In contrast, one cannot draw the categorical conclusion that all doses above the mixtures RfD or RSD are unacceptable, nor that all doses at or below these values are acceptable. As discussed in Barnes and Dourson (1988), as the frequency of exposures exceeding the RfD increases, the probability that adverse effects may be observed in the human population increases. Such an increase is not a certainty.

Another potential difficulty with the proposed fish consumption advisory (and existing advisories as well) lies with the use of RfDs or RSDs for a primary chemical which may be represented in fish flesh more by a metabolite or other secondary product that has an inherently different toxicity. This possibility certainly exists with PCBs. The RfD listed in Table 1 is that for Aroclor 1016, a relatively less-chlorinated mixture compared with other PCB mixtures. Since the toxicity in our examples is dominated by PCBs, it might be useful to establish additional RfDs for PCBs other than Aroclor 1016.

The development of criteria is useful in the comparison of the potential health risk from different sites or situations (see Eq. 2 and Figs. 3 through 6). Criteria are developed for other media (e.g., air, water) routinely and are readily used in a mixtures risk assessment. Moreover, a methods text describing the development of criteria is now available (U.S. EPA, 1989). Although different data sets may measure chemical concentrations in fish by different methods (i.e., whole fish versus skin-on fillets), these difficulties may be discounted in part if criteria are used only for comparisons among sites or situations with similarly derived data. For example, even a quick comparison of Figs. 4, 5, and 6 indicates that the fish from the Sheboygan River are by far the most contaminated. In each of these rivers, however, the toxicity hazard is dominated by PCBs.

Also of note is that concentration/criterion ratios calculated in Figs. 3 through 6 are dependent on the assumption of fish consumption used in the determination of the underlying criteria. In these examples an average fish consumption level of 20 g/day was used but a higher consumption rate, which would protect high-intake fish consumers, could also be applied (U.S. EPA, 1988a). Thus, the development of criteria, while useful for comparing the potential risks among sites, is not recommended in the development of fish consumption advisories since it is dependent upon the assumptions used for fish consumption. The proposed model for fish consumption advisories (Eq. 1) obviates this latter problem by establishing fish intake as the dependent variable.

In conclusion, we find that new health risk assessment information and risk assessment methods have not been considered in current fish consumption advisories. We recommend that future advisories use the latest data and methods and follow a model similar to that proposed here. We also recommend that environmental scientists develop criteria when they are interested in comparing the potential health risk among sites or situations. These recommendations will result in more scientifically credible fish consumption advisories and analyses among sites, and ultimately provide better protection of public health.

APPENDIX

The U.S. EPA has a recommended approach for conducting a chemical mixtures risk assessment (U.S. EPA, 1986). In any mixtures risk assessment, the first question that should be addressed after determining that adequate data are available is whether toxicity data exist on the mixture of concern or on a similar mixture. Such toxicity data on mixtures are sparse. Recently the U.S. EPA has compiled MIXTOX, a personal computer data base of studies on toxicity of mixtures and interacting chemicals (U.S. EPA 1988b). This data base can be accessed to provide data on mixtures.

If toxicity data on the mixture or on a similar mixture are not available, then a mixtures risk assessment may be conducted using toxicity data of components. In this paper a mixtures risk assessment was conducted on noncancer toxicity data of components.

A hazard index (HI) was calculated in each case in Figs. 3 through 6 by the following equation from U.S. EPA (1986):

$$\mathrm{HI} = E_1/\mathrm{AL}_1 + E_2/\mathrm{AL}_2 + \cdots E_i/\mathrm{AL}_i,$$

where E_i is the fish contaminant levels in milligrams of chemical per kilogram of fish as measured by DeVault *et al.*, Table 3, 1982 values (1986) (Fig. 3 in this paper), and DeVault (1985) (Figs. 4 through 6 in this paper); AL_i is the criterion as defined in Eq. 2; and where for all chemicals (i) the critical effect upon which the RfD is based is on the same target organ (e.g., liver).

As an example of how this works, refer to Fig. 3. A chemical mixtures risk assessment for the liver results in a mean value of 16 with a range of 15 to 19 [this range is based on the confidence limits of the DeVault *et al.* (1986) data] for the daily fish consumption of 20 g. The mean value is calculated as

$$\begin{aligned}\mathrm{HI} = {} & \mathrm{DDT}\ [2.74\ \mathrm{mg/kg\ divided\ by}\ 2\ \mathrm{mg/kg}] \\ & + \mathrm{dieldrin}\ [0.21\ \mathrm{mg/kg\ divided\ by}\ 0.2\ \mathrm{mg/kg}] \\ & + \mathrm{oxychlordane}\ [0.075\ \mathrm{mg/kg\ divided\ by}\ 0.2\ \mathrm{mg/kg}] \\ & + \mathrm{PCBs}\ [5.63\ \mathrm{mg/kg\ divided\ by}\ 0.4\ \mathrm{mg/kg}] \\ = {} & 1 + 1 + 0.4 + 14 \\ = {} & 16\ \mathrm{range\ of}\ 15\ \mathrm{to}\ 19.\end{aligned}$$

In Figs. 1 and 2 and Table 3 a slightly different mixtures risk assessment was performed, necessitated by the nature of the suggested fish consumption advisory (see Eq. 1). In these figures a mixtures RfD for a given target organ was first estimated by way of the following equations (Hertzberg, 1988): Assuming additivity (U.S. EPA, 1986) it follows that,

$$E_1/\mathrm{RfD}_1 + E_2/\mathrm{RfD}_2 + \cdots E_i/\mathrm{RfD}_i = \text{total contaminants (TC)}/\mathrm{RfD}_\mathrm{m},$$

where E_i is as before, RfD_m is the RfD for the mixture (mg of chemical/kg of body weight/day), and TC is the total contaminant load in the fish flesh (mg of chemical/kg of fish). By rearrangement one gets,

$$\mathrm{RfD}_\mathrm{m} = \text{total contaminants (TC)}/\textstyle\sum E_i/\mathrm{RfD}_i.$$

Once a mixtures reference dose (RfD_m) is estimated for a given target organ, it is multiplied by an assumed body weight in kilograms and then divided by the total concentration of contaminants affecting the given organ to yield the fish intake. As an example, refer to Fig. 1. An estimation of the RfD_m for the liver for lake trout of >25 in. in size results in a value of 0.0001 (i.e., 1E−4) mg/kg bw/day; that is,

$$\begin{aligned}\mathrm{RfD}_\mathrm{m} &= 6.96/[\text{chlordane } (0.54/5\text{ E}-5\text{ mg/kg/day}) + \text{DDT } (1.71/5\text{ E}-4\text{ mg/kg/day})\\ &\quad + \text{dieldrin } (0.12/3\text{ E}-5\text{ mg/kg/day}) + \text{PCBs } (4.59/1\text{ E}-4\text{ mg/kg/day})]\\ &= 0.0001\text{ mg/kg/day}.\end{aligned}$$

When this RfD_m is multiplied by 70 kg bw and then divided by the total concentration of contaminants affecting the liver calculated from Clark *et al.* (1987) as 6.9 mg of chemical/kg of fish [i.e., 0.54 (chlordane) + 4.59 (PCBs) + 1.71 (DDT) + 0.017 (dieldrin)], the result is the corresponding fish intake of 0.001 kg of fish/day:

$$\begin{aligned}\text{fish intake} &= 0.0001\text{ (mg/kg bw/day)} \times 70\text{ kg bw}/6.9\text{ mg/kg of fish}\\ &= 0.001\text{ kg of fish/day}.\end{aligned}$$

The range of the mixtures risk assessment per organ is based on similar derivations of mixtures RfDs associated with the standard deviations provided by Clark *et al.* (1987).

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