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DERIVATION OF WILDLIFE VALUES FOR MERCURY

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A procedure has been developed to estimate surface water concentrations of toxicants ("wildlife values") that will protect the viability of wildlife populations associated with aquatic resources. This procedure was designed primarily to protect piscivorous birds and mammals from compounds that bioaccumulate in fish and was used in the Great Lakes Water Quality Initiative (GLI) to calculate wildlife values (WV) for mercury, DDT/DDE, total polychlorinated biphenyls (PCBs), and 2,3,7,8-tetrachlorodibenzodioxin (TCDD). Published in 1995, and expressed as total mercury in unfiltered water, the final wildlife value (WV) for mercury derived in the GLI was 1300 pg Hg/L. This value was selected as the wildlife criterion (WC) for mercury in the Great Lakes basin. A second WV for mercury was derived in 1997 as part of a Congressionally mandated report on airborne mercury emissions. These calculations were based upon mercury speciation data that were largely unavailable when the GLI was developed. Important features of the WV_i in the Report to Congress include its calculation on a dissolved methylmercury basis and a reliance on field data to estimate fish bioaccumulation factors. Calculated as methylmercury in filtered water, the WV_i derived in the report is 50 pg Hg/L (equivalent to 54 pg MeHg/L). A comparison of WV in the GLI and the Report to Congress requires that average values be specified for mercury speciation in natural systems. Based on this information, the WV_i given in the report corresponds to a value of 910 pg Hg/L, as total mercury in unfiltered water, or about 70% of the WV_i derived in the GLI. In this article we describe the algorithm used to derive WV in the GLI and the Report to Congress and review its application to mercury. Scientific uncertainties in deriving WV, particularly as they apply to mercury, are critically examined.

In 1985, the U.S. Environmental Protection Agency (EPA) published an ambient water quality criterion for mercury to protect aquatic life in freshwater systems (U.S. EPA, 1985). This criterion was based upon the Food and Drug Administration (FDA) action level for mercury in fish (1 mg/kg), combined with knowledge of the extent to which methylmercury bio-

We acknowledge the efforts of those who were primarily responsible for developing the U.S. EPA procedure for calculation of WV, including Cynthia Nolt, Robert Pepin, Beth Goodman, and Jack Sullivan. We also thank the principal architects of the Report to Congress for their tireless support, especially Martha Keating, Kate Mahaffey, Rita Schoeny, Glenn Rice, Robert Ambrose, and Russ Bullock.

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concentrates in long-term laboratory exposures. Expressed as total acid-soluble mercury (filterable after acidification to pH 2), the value of this criterion is 12,000 pg Hg/L (4-d average concentration). This criterion does not explicitly distinguish between different mercury species in water. However, because it was calculated using a methylmercury bioconcentration factor (BCF), it was effectively based upon the assumption that all mercury in water exists as methylmercury. Effects on terrestrial wildlife were not considered in these calculations, although a review of toxicity information for mallard ducks (Heinz, 1979) led the authors to suggest that the criterion "might be an order of magnitude too high," that is, not protective of fish-eating waterfowl. This aquatic life criterion remains the primary national benchmark for evaluating mercury levels in U.S. surface waters.

More recently, the U.S. EPA addressed the possibility that mercury and other chemicals that accumulate in aquatic biota might pose a threat to terrestrial wildlife associated with aquatic resources. A procedure was developed to estimate chemical concentrations in surface waters that would protect wildlife populations. This procedure was subsequently used to derive "wildlife values" (WV) for mercury, total polychlorinated biphenyls (PCBs), 2,3,7,8-tetrachlorodibenzodioxin (TCDD), and DDT/DDE in the Final Water Quality Guidance for the Great Lakes System (Great Lakes Water Quality Initiative [GLI]; U.S. EPA, 1995a). WV were calculated for several piscivorous birds and mammals. Species-specific values were then averaged to obtain avian and mammalian values. For mercury, the avian and mammalian WV were 1300 and 2400 pg Hg/L, respectively, as total mercury in unfiltered water. The lower of these two values was selected as the "wildlife criterion" (WC) for mercury. States in the Great Lakes basin are presently implementing strategies for compliance with the GLI, including the WC contained therein.

Coinciding with the development of the GLI, but otherwise unrelated from a regulatory perspective, Congress requested in 1990 that the U.S. EPA submit a study on atmospheric mercury emissions [the request appears in Section 112(n)(1)(B) of the 1990 Amendments to the Clean Air Act]. The emissions sources to be covered in this study included electric utility steam generating units, municipal waste combustion units, and chlor-alkali facilities. Congress directed that this study evaluate the rate and mass of mercury emissions, health and environmental effects, technologies to control such emissions, and the costs of such controls. In fulfillment of this request, the U.S. EPA submitted the Mercury Study Report to Congress ("Report to Congress" or "Report") in December 1997 (U.S. EPA, 1997). An important contribution of the Report to Congress was to recalculate WV for mercury using recently published speciation data. These calculations were performed using methylmercury bioaccumulation factors (BAFs) estimated directly from field data. Variability in BAF estimates arising from these sources was addressed by using a Monte Carlo

simulation approach. Calculated as methylmercury in filtered water, the avian and mammalian WV published in the Report to Congress were 74 and 50 pg Hg/L, respectively.

The purpose of this article is to describe the procedure for deriving WV, as it has been applied to mercury. Scientific uncertainties associated with the WV methodology are reviewed. An emphasis is placed on uncertainties that pertain directly to mercury, although most would apply to any assessment of bioaccumulative compounds in piscivorous wildlife. Special attention was given to information that may aid in the interpretation of existing toxicity information for mercury and provide a rational basis for the selection of uncertainty factors.

PROCEDURE FOR THE DERIVATION OF WILDLIFE VALUES

The WV for mercury in the GLI was defined as the concentration of total mercury in the water column that, if not exceeded, protects wildlife that use the water as a drinking or foraging source. This definition was interpreted to mean the highest concentration of mercury that causes no significant reduction in growth, reproduction, viability or usefulness (in a commercial or recreational sense) of a population of animals exposed over multiple generations. The WV for mercury in the Report to Congress was interpreted in a similar manner, but was calculated instead as methylmercury in filtered water, including both freely dissolved methylmercury and methylmercury that is associated with dissolved organic material. It is important to note that by convention mercury concentrations in environmental media and dosing formulations are generally expressed as micrograms of elemental mercury ($\mu\text{g Hg/g}$), regardless of the identity of the mercury species. This convention is retained throughout the present analysis unless otherwise indicated.

The equations used to calculate WV for mercury in GLI and in the Report to Congress are essentially identical:

$$\text{WV} = \frac{\{\text{TD} \times [1/(\text{UF}_L \times \text{UF}_A \times \text{UF}_S)]\} \times \text{Wt}_A}{\text{W}_A + [(\text{FD}_3 \times \text{F}_A \times \text{BAF}_3) + (\text{FD}_4 \times \text{F}_A \times \text{BAF}_4)]}$$

where:

WV = wildlife value (pg Hg/L; after converting from $\mu\text{g Hg/L}$)

Wt_A = average species weight (kg)

W_A = average daily volume of water consumed (L/d)

F_A = average daily mass of food consumed (kg/d)

FD_3 = fraction of the diet derived from trophic level 3

FD_4 = fraction of the diet derived from trophic level 4

BAF_3 = aquatic life bioaccumulation factor for trophic level 3

(L/kg; methylmercury concentration in fish/methylmercury in water)

BAF_4 = aquatic life bioaccumulation factor for trophic level 4
(L/kg; methylmercury concentration in fish/methylmercury
in water)

TD = tested dose from toxicity studies with wildlife species
($\mu\text{g Hg/kg body weight/d}$)

UF_L = LOAEL-to-NOAEL uncertainty factor

UF_A = species-to-species uncertainty factor

UF_S = subchronic-to-chronic uncertainty factor

This equation explicitly accounts for scientific uncertainty in three different areas, each of which is described later.

A similar equation was first used by the State of Wisconsin to set Wild and Domestic Animal Criteria (State of Wisconsin, 1989). The approach was later modified by the U.S. EPA and used to develop interim WW for four compounds (mercury, total PCBs, TCDD, and DDT/DDE) in support of the Proposed Water Quality Guidance for the Great Lakes System (U.S. EPA, 1993a, 1993b). The Final Guidance was developed from the Proposed Guidance after responding to public comment (U.S. EPA, 1995a) and peer review by the U.S. EPA Science Advisory Board (U.S. EPA, 1992). Separate technical support documents provide the scientific basis for estimating BAFs (U.S. EPA, 1995d) and calculating WW (U.S. EPA, 1995b, 1995c). The procedure for deriving WW was evaluated in 1992 at a national workshop sponsored by the U.S. EPA (U.S. EPA, 1994a). The method was also reviewed by the U.S. EPA Science Advisory Board in 1994 in terms of its application as a national methodology (U.S. EPA, 1994b). Detailed descriptions of the method, including comparisons with other proposed methods for deriving WW, are presented elsewhere (U.S. EPA, 1993b, 1994a, 1995c).

An examination of the equation reveals an effect (numerator) and an exposure (denominator) component. In both the GLI and the Report to Congress, toxicity testing data were reviewed in an effort to identify chronic NOAELs (no-observed-adverse-effect levels) for use as the tested dose (TD). The procedure provides that in the absence of a NOAEL, a LOAEL (lowest-observed-adverse-effect level) may be used with the addition of a factor (UF_L) to account for uncertainty around the toxic threshold. A second uncertainty factor (UF_A) may be used to account for interspecies uncertainty when extrapolating data from a species other than the species of concern, and a third uncertainty factor (UF_S) may be employed to extrapolate from subchronic to chronic exposures. Additional adjustments are permitted if they are justified by toxicokinetic or toxicodynamic considerations. Division of the TD by the product of all three UFs results in the estimation of a wildlife reference dose (RfD), which is then used to calculate the WW. An excellent discussion of uncertainty factors as they relate to toxicity extrapolations with terrestrial wildlife was developed to support the derivation of WW (Abt Associates, 1995). A more general discussion of uncertainty factors can be found in a recent review (Chapman et al., 1998).

In the GLI, species-specific WW (WW_s) were calculated for the bald eagle (*Haliaeetus leucocephalus*), herring gull (*Larus argentatus*), belted kingfisher (*Ceryle alcyon*), mink (*Mustela vison*), and river otter (*Lutra canadensis*). These species were selected after consideration of (1) their exposure to bioaccumulative contaminants, (2) relevance to Great Lakes ecosystems, (3) availability of information with which to calculate WW, and (4) evidence for accumulation and/or adverse effects. Intermediate WW (WW_i) were then obtained for avian and mammalian wildlife by calculating the geometric mean of values for contributing species. A wildlife criterion (WC) was set equal to the lowest of the two intermediate values and, for mercury, was driven by the calculations for avian species.

For the Report to Congress, a decision was made to replace the herring gull with the osprey (*Pandion haliaetus*) and common loon (*Gavia immer*). The basis for this decision was a desire to consider birds that were distributed over a larger geographical area, consistent with the national-scale focus of the Report. In addition, the toxicity of mercury to loon populations had been previously demonstrated following point-source contamination of the English River–Wabigoon system in northern Ontario (Barr, 1986) and studies evaluating the effects of mercury on loons in northern Wisconsin inland lakes were ongoing at the time (Meyer et al., 1995).

EFFECTS OF MERCURY ON AVIAN AND MAMMALIAN WILDLIFE

The toxicity of mercury depends on the chemical species in question. Mercury can exist in an elemental form, as inorganic mono- or divalent mercury, or as any one of several organic forms. Of the possible organic forms that may be present in natural systems, methylmercury generally predominates. Both inorganic mercury and methylmercury can accumulate in aquatic biota. However, the proportion of total mercury that exists as the methylated form tends to increase with trophic level, generally approaching 100% at trophic levels 3 and 4 (May et al., 1987; Watras & Bloom, 1992; Bloom, 1992; Becker & Bigham, 1995; Mason & Sullivan, 1997). It is appropriate, therefore, to focus attention on the toxicity of methylmercury to piscivorous avian and mammalian wildlife. Reviews of mercury toxicity to wildlife species are provided in a support document for the GLI (U.S. EPA, 1995b) and in the Report to Congress (U.S. EPA, 1997, Vol. VI). The toxicity of mercury to birds has also been reviewed by Scheuhammer (1987). The authors of the GLI evaluated 65 studies on the toxicity of mercury to birds and mammals. Studies used to calculate TD values were then selected after considering factors such as study duration, toxicity endpoints, and the number and spacing of dose groups. Preference was also given to studies that employed “wildlife” species, as opposed to more traditional laboratory test animals. The authors of the Report reviewed literature published after the GLI was written and concluded that there were no new studies that could be used to calculate a TD for avian

or mammalian wildlife. It is not our intent to duplicate these efforts. Instead, a brief summary of methylmercury toxicity to vertebrate systems is presented, with the goal of providing guidance on the selection of appropriate toxicological endpoints. Detailed descriptions of studies with wildlife are limited to the studies that were used to establish TD values in both the GII and the Report to Congress. As is evident from these descriptions the most comprehensive studies of methylmercury toxicity to wildlife were published more than 20 years ago.

Mechanism of Toxicity

Methylmercury in the diet is absorbed with high efficiency in the vertebrate digestive tract and associates rapidly with sulfhydryl-containing molecules in blood, including both free amino acids and glutathione (Carty & Malone, 1979). These mobile complexes transport methylmercury to tissues and organs, and facilitate its movement across cell membranes. In particular, there is good evidence for saturable transport of methylmercury–cysteine complexes across both the blood–brain and placental barriers (Kerper et al., 1992; Kajiwara et al., 1996). The transport of methylmercury–glutathione complexes across the liver canalicular membrane may contribute to the excretion of methylmercury into bile (Dutczak & Ballatori, 1994). Although it exhibits a range of toxic effects in several target tissues, the primary effects of methylmercury are on the central nervous system. Neurotoxicity occurs in both adults and developing animals. In the latter case, this effect appears to be linked to a disturbance of microtubule function in dividing cells, resulting in antimitotic activity (Rodier, 1995). The mode of action of methylmercury in the differentiated nervous system is less well known, but may involve selective effects on astrocytes and other neuroglial cells (Cranmer et al., 1996).

In chronic toxicity studies with mammals, including humans, the most sensitive indicator of methylmercury intoxication is cognitive impairment of animals exposed in utero (U.S. EPA, 1997, Vol. V). In general, the sophisticated methods employed in such studies have not been used in studies with avian or mammalian wildlife species. Instead, less “subtle” endpoints are generally employed, including decreased reproduction and impaired mobility. It is difficult, therefore, to establish the relative “sensitivity” of different endpoints in studies with wildlife or to speculate on the potential utility of behavioral observations. Moreover, efforts to distinguish between endpoints can be complicated by interactive effects. For example, reproductive impacts can occur as a result of direct effects on the developing nervous system, impaired behavior of adults (e.g., unsuccessful matings or diminished quality of parental caregiving), or both.

Toxicity Tests With Mallard Ducks

A comprehensive study of methylmercury toxicity to mallard ducks was undertaken by Heinz (1974, 1975, 1976a, 1976b, 1979), and involved

three generations of ducks fed methylmercury dicyandiamide (0, 0.5, and 3 $\mu\text{g Hg/g}$, spiked into the diet). In the first generation, treatment began in adult ducks. Subsequent generations received treatment beginning at 9 d of age. Adverse reproductive effects on the first generation of ducks were observed at the 3 $\mu\text{g/g}$ dosing level, but not in ducks fed 0.5 $\mu\text{g/g}$ (Heinz, 1974). In a later study, reproduction in first- and second-generation ducks was evaluated (Heinz, 1976a, 1976b). As before, there were no apparent effects on first-generation ducks at the 0.5 $\mu\text{g/g}$ dosing level; however, second-generation animals dosed at this level suffered adverse reproductive effects including eggs laid outside the nest box, reduced number of offspring surviving to 1 wk of age, and reduced growth of offspring. A third generation of mallards also suffered adverse reproductive effects at 0.5 $\mu\text{g/g}$ mercury in the diet, including a reduction in the number of viable eggs laid per day and thinner eggshells.

Heinz (1975, 1979) also examined the effects of mercury on the approach response of chicks to maternal calls and avoidance of frightening stimuli. In third-generation ducklings born to parents dosed with 0.5 $\mu\text{g/g}$ mercury there was a reduction in the response rate and speed of response to maternal calls. When data were pooled from all studies and subjected to analysis of variance (ANOVA) with multiple comparisons, altered behavior was demonstrated in the lowest dosed groups in all generations (0.5 $\mu\text{g/g}$). These alterations included a reduction in the number of ducklings that approached maternal calls and an increase in the distance traveled to avoid a threatening stimulus.

Toxicity Tests With Ranch Mink

The effects of dietary methylmercury on ranch mink were studied by Wobeser et al. (1976a, 1976b). The study consisted of two experiments, which together formed the basis of Wobeser's PhD dissertation (Wobeser, 1973). In the first experiment (Wobeser et al., 1976a), adult female mink and their litters were fed an uncontaminated control diet or a ration containing mercury-contaminated freshwater drum from Lake Winnipeg, Manitoba. The fish was supplied in a ground, frozen form and was mixed with cereal and uncontaminated feed to a desired composition of 50 or 75 kg fish/100 kg food. All mink were fed once daily in slight excess of consumption, and the 3 exposure groups were observed for 145 d. One female and 3 to 6 kits were euthanized every 15 (treatment) or 30 (control) d. Complete necropsies were then performed. No clinical signs of disease were observed in any of the mink within the experimental period, and no mortality or growth impairment occurred that could be attributed to the feeding of mercury-contaminated fish.

In the second experiment (Wobeser et al., 1976b), adult female mink were given feed spiked with methylmercuric chloride at 0.0 (control), 1.1, 1.8, 4.8, 8.3, or 15 $\mu\text{g Hg/g}$. Two mink from each group were allowed to die of intoxication or were euthanized after 93 d (the end of the experi-

ment). Animals were necropsied and the tissues analyzed for mercury content. All animals in the control group remained clinically normal, and the only clinical sign in the 1.1- $\mu\text{g/g}$ dose group was a slight tendency for two of the animals to move more slowly than the others during the last few days of the experiment. Anorexia, posterior ataxia, and lateral recumbency were observed in the other four dose groups. Death occurred within 26–36 d at 4.8 $\mu\text{g/g}$, and within 19–26 d at 8.3 $\mu\text{g/g}$. Histopathological abnormalities were seen at 1.1 $\mu\text{g/g}$, including pale, yellow livers, lesions in the central nervous system, and axonal degeneration. Importantly, it was the author's opinion that these nervous tissue abnormalities would have become manifested as impaired motor function had the exposures been carried out for a longer period of time.

Factors Relevant to the Interpretation and Use of Mercury Toxicity Data

Very few studies of methylmercury toxicity to wildlife have been conducted, and the extent to which these results can be extrapolated among species and from the laboratory to the field remains in question. Two inter-related issues that contribute substantially to this uncertainty are hepatic demethylation of methylmercury and the protective effects of dietary selenium. Interactions between mercury and selenium have been known for many years. Koeman et al. (1973) found that mercury and selenium occurred in a 1:1 molar ratio in the livers of several marine mammal species and that most of this mercury existed in an inorganic form. Correlations between mercury and selenium in liver tissue have also been reported for several piscivorous seabirds, although the Se:Hg ratio tends to be lower than 1:1 (Elliot et al., 1992). In feeding studies, sodium selenite protected against methylmercury toxicity to Japanese quail (Stoewsand et al., 1974) and rats (Ganther et al., 1972; Chang & Suber, 1982), leading to the suggestion that selenium protects human consumers from high levels of methylmercury in tuna, swordfish, and other seafood products (Grandjean et al., 1992). Selenium is known to bind mercury after hepatic demethylation of methylmercury. The compounds formed in this manner probably include both mercury-selenoproteins and inorganic Se–Hg complexes (Palmisano et al., 1995; Cavalli & Cardellicchio, 1995) and are almost certainly less toxic than parent methylmercury. Particularly high levels of inorganic mercury have been measured in livers taken from marine mammals and from the carnivorous polar bear (Dietz et al., 1990), and it has been speculated that hepatic demethylation confers protection to animals that consume large quantities of fish or, in the case of the polar bear, fish-eating seals (Wren et al., 1986).

Birds and mammals that inhabit freshwater ecosystems also appear to be capable of demethylating methylmercury. Methylmercury constituted 46% of total mercury in the livers of mink fed a diet of methylmercury-contaminated fish, although there was no apparent relationship between

concentrations of liver mercury and selenium (Jernelöv et al., 1976). Similar speciation patterns were reported by Wren et al. (1986) for livers taken from mink (53% methylmercury) and otter (34%). Barr (1986) found that methylmercury comprised 4% to 27% of total mercury in livers of loons collected from a mercury-contaminated watershed in northern Ontario. Interestingly, the percentage of methylmercury did not vary with the gradient of site contamination, as might have been expected if the demethylation pathway saturated at particularly high exposure levels. A positive correlation between liver mercury and selenium was reported in the goldeneye, but no attempt was made to identify mercury species (Eriksson et al., 1989).

Speciation data provided by Fimreite (1974) suggests that in ducks the activity of this demethylating pathway is related to fish consumption as a proportion of the diet. Among adult ducks, fish-eating mergansers exhibited the lowest levels of methylmercury in liver as a percent of total (12%). Methylmercury constituted 32%, 38%, and 52% of total mercury in the livers of goldeneyes, mallards, and pintails, respectively. This detoxifying ability appears to develop early in life. In livers taken from ducklings, methylmercury as a percent of total averaged 27%, 49%, 53%, and 58% in the merganser, mallard, goldeneye, and pintail. Methylmercury levels in breast muscle from adults of all four species were essentially identical, averaging about 60% of total. In the context of deriving WV for mercury, these observations are important for two reasons: (1) The toxicity of methylmercury to birds and mammals in the laboratory and in the environment may depend upon the availability of dietary selenium; and (2) most of the toxicity tests with birds conducted to date have been performed using non-piscivorous species that may not possess a well-developed demethylating capability.

As indicated previously, the disposition of methylmercury also appears to be controlled by carrier-mediated transport of methylmercury complexes with cysteine and glutathione. Presently, the activity of these pathways in wildlife species is essentially unknown, and there is no information whatsoever on these pathways in birds. As more information on demethylation and transport of methylmercury becomes available, intraspecific differences in these mechanisms may yield explanations for apparent differences in sensitivity among species.

ESTIMATED BIOACCUMULATION FACTORS FOR MERCURY

In both the GLI and the Report to Congress, mercury BAFs were expressed by making the simplifying assumption that aquatic food chains can be adequately represented using four trophic levels. Respectively, these trophic levels are: level 1, phytoplankton (algal producers); level 2, zooplankton (primary herbivorous consumers); level 3, small forage fish (secondary consumers); and level 4, larger, piscivorous fish (tertiary consumers). This type of food chain typifies the pelagic assemblages found in

large freshwater lakes and has been used extensively to model the bioaccumulation of hydrophobic organic compounds (Gobas, 1993). It was recognized, however, that food chain structure and length can vary considerably among aquatic systems resulting in differences in mercury bioaccumulation for a single species of fish (Cabana et al., 1994). In addition, this simplified structure ignores several important groupings of organisms, including benthic detritivores, macroinvertebrates, and herbivorous fishes.

The GLI provided a hierarchy of methods for deriving BAFs for mercury and other bioaccumulative compounds. In descending order of preference, the methods given were (1) direct measurement from chemical residues in fish, preferably collected from the Great Lakes basin, (2) multiplication of a laboratory-derived BCF by a food-chain multiplier appropriate to each trophic level, and (3) multiplication of a model-derived BCF by the same food-chain multipliers used in method 2. The authors of the GLI concluded that field data were insufficient to directly estimate BAFs for mercury. In particular, there were few reliable measurements of mercury concentration in water available at the time that could be paired with measured residues in fish, and virtually no such measurements for Great Lakes fishes. BAFs for mercury were therefore calculated using the $BCF \times$ food chain multiplier method. Based on a review of available speciation data, methylmercury was assumed to make up 97.5% of total mercury in fish and 17% of total mercury in water. These assumptions were then applied to existing bioconcentration data to obtain a weighted average BCF for total mercury of approximately 11,360. Food-chain multipliers for trophic levels 2 and 3 were set equal to 2 and 2.52, respectively, based on values determined in a single study by Watras and Bloom (1992). The food-chain multiplier for trophic level 4 was set equal to 12.6 (2.52×5) and was supported by several studies of mercury residues in large piscivorous fish and their prey. Multiplying these values by the laboratory-derived BCF yielded BAFs of approximately 27,900 and 139,530 for trophic levels 3 and 4 (total mercury in fish divided by total mercury in unfiltered water).

In the Report to Congress, BAFs were based entirely on published field data and were calculated on a methylmercury basis (U.S. EPA, 1997, Vol. III, App. D). BAFs for trophic level 3 were calculated in two ways: (1) from measured methylmercury concentrations in forage fish and water ("field-derived"), and (2) as the product of measured residues in phytoplankton (BCF for trophic level 1) and a food-chain multiplier representing biomagnification at trophic levels 2 and 3 (FCM_{1-3}). BAFs for trophic level 4 were calculated in three ways: (1) from measured methylmercury concentrations in large piscivorous fish; (2) as the product of measured residues in phytoplankton and a food-chain multiplier representing biomagnification at trophic levels 2, 3, and 4 (FCM_{1-4}); and (3) as the product of measured residues in forage fish (BAF_3) and a food-chain multiplier representing biomagnification at trophic level 4 (FCM_{3-4}).

An effort was made in the Report to characterize statistical distributions

for each of the variables used in BAF calculations. This variability was then explicitly treated using a repeated sampling (Monte Carlo) procedure. Results of the Monte Carlo simulations for each of the methods are given in Table 1. There is a large variance in all of the distributions, which cannot be separated into variability in BAFs and uncertainty in their estimation. The BAFs recommended in the Report were the median values developed from measured methylmercury concentrations in fish at trophic levels 3 and 4, rounded off to the nearest 100,000. Only four data points were available to characterize the BAF₃ and BAF₄ distributions. In each case, however, these data points were in relatively good agreement, resulting in narrower statistical distributions than those associated with the other approaches.

EXPOSURE PARAMETERS

Exposure parameters used to calculate WV in the Report to Congress are shown in Table 2. Parameters assigned to the mink and otter are identical to those used in the GLI and were based on the same scientific guidance (U.S. EPA 1993c, 1995c). In contrast, parameters assigned to the bald eagle differ somewhat from those used in the GLI due to differences in the geographical focus of each effort. Based upon published observations for eagles in the Great Lakes basin, the authors of the GLI assumed that mercury-contaminated herring gulls constituted 6% of the diet of bald eagles. An additional 2% of the diet was assumed to consist of "nonaquatic" birds. Because the Report to Congress was intended to be a nationwide assessment, use of this region-specific assumption was not considered appropriate. Eagles were therefore assumed to consume nonfish prey, with no mercury contamination, as 8% of the total diet. The ingestion rate for kingfishers also differs from that used in the GLI (0.067 kg/d). The value used in

TABLE 1. Summary of Methylmercury Bioaccumulation Factors for Trophic Levels 3 and 4 Given in the Report to Congress (Median, 5%, and 95% Values)

Recommended	BAF ₃ 1,600,000		BAF ₄ 6,800,000		
	Field-derived	BCF × FCM ₁₋₃	BAF ₃ × FCM ₃₋₄	Field-derived	BCF × FCM ₁₋₄
50th Percentile (GM ^a)	1,580,000	1,320,000	7,820,000	6,810,700	6,520,000
5th Percentile	461,000	7,000	1,960,000	3,260,000	330,000
95th Percentile	5,410,000	24,400,000	31,100,000	14,200,000	129,000,000
GSD ^b	2.15	5.88	2.32	1.56	6.13

^aGeometric mean; defined as e^{μ} , where μ is the mean of the natural logarithms of the observations. All of the percentiles are given as the geometric equivalents (antilogos) of the actual values generated by the simulations.

^bGeometric standard deviation; defined as e^{σ} , where σ is the standard deviation of the natural logarithms of the observations.

TABLE 2. Exposure Parameters for Wildlife Species Evaluated in the Report to Congress

Species	Body weight, WtA (kg)	Ingestion rate, F_A (kg/d)	Drinking rate, W_A (L/d)	Trophic level of wildlife food source	Percent of diet at each trophic level	Percent of diet from nonaquatic sources ^a
Mink	0.80	0.178	0.081	3	90	10
Otter	7.40	1.220	0.600	3, 4	80, 20	0
Kingfisher	0.15	0.075	0.017	3	100	0
Loon ^b	4.00	0.800	0.120	3	100	0
Osprey ^b	1.50	0.300	0.077	3	100	0
Eagle	4.60	0.500	0.160	3, 4	74, 18	8

^aAssumed in the Report to Congress to be uncontaminated by mercury.

^bThese species not evaluated in the GLI.

the Report was originally set equal to that given in the Proposed Water Quality Guidance and, due to an oversight, was not changed when the GLI was published. The weight of loons was calculated in the Report as the average of values reported by Barr (1986) for adult males and females, and the feeding rate was taken from Barr (1973). Data provided by Barr (1996) suggested that when given the opportunity loons feed almost exclusively on live fish, and that nearly all of these fish belong to trophic level 3. Exposure parameters for the herring gull are not given in Table 2. In the GLI the herring gull was assumed to derive 72% of its diet from trophic level 3, 18% from trophic level 4, and 10% from nonaquatic (uncontaminated) sources.

CALCULATION OF WILDLIFE RfDs

The avian RfDs calculated in both the GLI and the Report to Congress were derived from studies by Heinz (1974, 1975, 1976a, 1976b, 1979) in which three generations of mallard ducks (*Anas platyrhynchos*) were dosed with methylmercury dicyandiamide. For the determination of a threshold dose (TD), it was concluded that reproductive and behavioral impacts on second- and third-generation ducks constituted adverse toxicological effects. These effects were observed when adult ducks were fed 0.5 μg Hg/g. The feeding rate of 156 mg/g/d given by Heinz (1979) was assumed in both analyses, resulting in a chronic LOAEL for mallards of 78 μg Hg/kg body weight/d. Because the mallard studies did not yield a NOAEL, the authors of the GLI adjusted the TD downward using a UF_L of 2. Selection of this UF_L was based on an interpretation of the dose-response relationships in the mallard study and an analysis of mercury toxicity data from selected laboratory studies (see LOAEL-to-NOAEL uncertainty factor, discussed later). A similar analysis led the authors of the Report to Congress to adjust the TD by a UF_L of 3. The estimation of an avian RfD also required an evaluation of interspecies differences between the mallard duck and piscivo-

rous birds of interest. A UF_A of 3 was employed in the GLI, based on the apparent sensitivity of mallards to methylmercury when compared to other bird species tested. The authors of the Report elected instead to apply a UF_A of 1 (i.e., no adjustment), based on the conclusion that piscivorous birds possess a greater capability to detoxify methylmercury than do nonpiscivorous birds (see earlier subsection, Factors Relevant to the Interpretation and Use of Mercury Toxicity Data).

Mammalian RfDs in both the GLI and the Report to Congress were derived from studies with mink conducted by Wobeser et al. (1976a, 1976b). In the GLI, the NOAEL for mink was determined to be 1.1 $\mu\text{g Hg/g}$. However, histopathological lesions in animals dosed at this level were considered to be evidence that a longer exposure would have elicited signs of toxicity. Consequently, the 1.1- $\mu\text{g Hg/g}$ dosing level was designated a subchronic NOAEL and a UF_S of 10 was employed to extrapolate this value to a lifetime exposure. In contrast to the GLI, histopathological lesions observed at the 1.1- $\mu\text{g Hg/g}$ dosing level were interpreted in the Report as evidence of an adverse toxic effect. The dose of 0.33 $\mu\text{g Hg/kg}$ (derived from contaminated fish) was therefore identified as the subchronic NOAEL. However, because these lesions were not associated with any overt signs of toxicity, the authors felt justified in using a UF_S of 3 to extrapolate to a lifetime exposure. In both the GLI and the Report to Congress the UF_A for extrapolation to wild mink was set equal to 1. Otter were considered to be sufficiently similar to mink that a UF_A of 1 was also considered appropriate.

A second difference between the GLI and the Report exists with respect to the assumed feeding rate and average weight of mink used in the Wobeser et al. (1976a, 1976b) studies. Based on a review of the literature for wild mink, the authors of the GLI used an average weight of 1 kg and a feeding rate of 0.15 kg/d. Converting, the 1.1- $\mu\text{g Hg/g}$ dosing level identified as the subchronic NOAEL corresponds to a mercury ingestion rate of 180 $\mu\text{g Hg/kg body weight/d}$. The authors of the Report instead assumed a food consumption rate of 0.16 kg/d reported for captive mink (Bleavins & Aulerich, 1981) and the average weight of animals (0.8 kg) reported by Wobeser et al. (1976a, 1976b). Adopting these values, the 0.33 $\mu\text{g Hg/g}$ dose level corresponds to a dosing rate of 55 $\mu\text{g Hg/kg body weight/d}$.

Wildlife RfDs were calculated in both efforts as the TD divided by the product of all applicable UFs. Based on the foregoing information, the wildlife RfDs given in the GLI were:

Avian species: 13 $\mu\text{g Hg/kg body weight/d}$

Mammalian species: 16 $\mu\text{g Hg/kg body weight/d}$

Similarly, the wildlife RfDs derived in the Report to Congress were:

Avian species: 26 $\mu\text{g Hg/kg body weight/d}$

Mammalian species: 18 $\mu\text{g Hg/kg body weight/d}$

DERIVATION OF WILDLIFE VALUES

WW derived in the GLI were calculated on a total mercury basis using the algorithm and inputs described previously. A sample calculation for the kingfisher is provided:

$$WW_s = \frac{(TD \times [1/(UF_A \times UF_S \times UF_L)]) \times Wt_A}{W_A + [(1.0) (F_A \times BAF_3)]}$$

$$WW_s = \frac{(0.078 \text{ mg/kg/d} \times [1/(3 \times 1 \times 2)]) \times 0.15 \text{ kg}}{0.017 + [(1.0) (0.067 \times 27,900)]}$$

$$WC_s = 1040 \text{ pg/L}$$

Similar calculations for the herring gull, eagle, mink, and otter yielded WW_s of 1190, 1920, 1930, and 2880 pg Hg/L, respectively. Calculated as the geometric mean of WW_s for mink and otter, the WW_i for mammals was determined to be 2400 pg Hg/L. The mean of WW_s for avian species was found to be 1300 pg Hg/L. Selecting the lowest of these average values, the authors of the GLI determined the WC for mercury to be 1300 pg Hg/L (as total mercury in unfiltered water).

Similar calculations were performed in the Report to Congress to generate WW for mercury on a methylmercury basis. Calculated as methylmercury in filtered water, WW_s derived for the kingfisher, osprey, loon, eagle, mink, and otter were 33, 82, 82, 100, 57, and 42 pg Hg/L, respectively. The geometric mean of WW_s for avian species was 74 pg Hg/L. The WW_i for mammals was 50 pg Hg/L. In contrast to the GLI, the derivation of a WW_i for mercury in the Report to Congress was driven by the calculations for mammals. Expressed as an aqueous concentration of methylmercury, the WW_i derived in the Report corresponds to a WW_i of 54 pg MeHg/L.

An estimate of the total dissolved mercury concentration corresponding to the WW_i in the Report to Congress can be obtained if it is assumed that dissolved methylmercury constitutes a fixed fraction of total dissolved mercury. Mercury speciation data from filtered water samples were given in the Report (U.S. EPA, 1997, Vol. III, App. D). Based upon an analysis of these data, it was suggested that methylmercury averages about 7.8% of total mercury in the surface water (the epilimnion) of lakes. Adopting this value, a methylmercury concentration of 50 pg Hg/L corresponds to a total dissolved mercury concentration of 641 pg Hg/L. An additional correction is needed if the WW_i is to be expressed as the corresponding amount of total mercury in unfiltered water. Published reports suggest that on average, total dissolved mercury comprises about 70% of the total mercury in unfiltered water samples (Back & Watras, 1995; Driscoll et al., 1995; Watras et al., 1995; Mason & Sullivan, 1997). Therefore, a total dissolved mercury concentration of 641 pg Hg/L corresponds to a total mercury concentration in unfiltered water of 910 pg Hg/L. Thus, when expressed as total mercury in

unfiltered water, the WV_f derived in the Report is approximately 70% of the WC derived in the GLI. Additional information can be obtained by similar conversions of the WV_s given in the Report. Where comparisons among species are possible, all of the WV_s calculated in the Report are lower than those published in the GLI, but differ by less than a factor of three.

As noted previously, the algorithms used to derive mercury WV in the GLI and the Report to Congress are essentially identical, and wildlife RfDs derived in both efforts were calculated using the same toxicity testing information. Differences that exist between these efforts are due, therefore, to the use of more recent mercury speciation data in the Report, and to differences in the interpretation of older data. In several instances, these differences in interpretation resulted in the use of different UFs and/or TD values to derive RfDs. For example, in the GLI, the TD identified for avian species was adjusted using a UF_A of 3 and a UF_L of 2, while in the Report to Congress the RfD for avian species was calculated using a UF_A of 1 and a UF_L of 3. This difference alone was sufficient to shift the overall analysis from one driven by the WV_i for avian species (GLI) to one in which the WV_f was determined by the WC_i for mammals (Report). Differences between the GLI and the Report with respect to calculation of a mammalian RfD tended to be offsetting. The TD identified in the GLI was approximately three times higher than that used in the Report to Congress (i.e., the next higher dose level). In calculating the mammalian RfD, however, the GLI used a UF_L of 10, while the Report employed a UF_L of 3. The overall result of these manipulations was that the RfD for mammals in the GLI differs from that in the Report only because of differences in the average weight and feeding rate assigned to mink used in the Wobeser et al. (1976a, 1976b) study.

The most important difference between the GLI and the Report to Congress lies in their respective use of mercury BAFs. Assuming that methylmercury constitutes 7.8% of total mercury in filtered water and that 70% of total mercury in unfiltered water is dissolved, it is possible to calculate total mercury BAFs corresponding to the methylmercury-based values used in the Report (Table 1). The calculated values are approximately 87,400 and 371,300 for trophic levels 3 and 4, respectively (methylmercury in fish divided by total mercury in unfiltered water). By comparison, the GLI used BAFs of 27,000 and 140,000 for trophic levels 3 and 4 (total mercury in fish divided by total mercury in unfiltered water). Assumptions about the percent of total mercury in fish that exists as methylmercury (the GLI assumed a value of 97.5%, while the Report adopted a value of 100%) contribute little to these differences.

MERCURY RESIDUES IN FISH CORRESPONDING TO WILDLIFE VALUES

Methylmercury concentrations in fish corresponding to the WV_f derived in the Report to Congress can be calculated by multiplying the WV_f by trophic level-specific BAFs. Employing the recommended BAFs pre-

sented in Table 1, a WV_f of 50 pg Hg/L corresponds to methylmercury concentrations in fish of 0.077 $\mu\text{g Hg/g}$ and 0.346 $\mu\text{g Hg/g}$ for trophic levels 3 and 4, respectively. Since all of the mercury in fish was assumed to exist as methylmercury, these values are directly comparable to total mercury residues reported for fish in the Report and elsewhere. Similar calculations can be attempted using the WC derived in the GLI and field-derived BAFs for fish expressed on a total (dissolved and particulate) mercury basis. A compilation of total dissolved mercury BAFs appears in the Report to Congress (U.S. EPA, 1997, Vol. III, App. D). Geometric mean BAFs for trophic levels 3 and 4, estimated using a Monte Carlo simulation method, were reported to be 119,000 and 496,000, respectively. A correction is required if these BAFs are to be expressed on a total mercury basis. In the previous section it was noted that total dissolved mercury averages about 70% of total mercury, including both dissolved and particulate forms. Adopting this value and correcting gives total mercury BAFs of 83,300 and 347,200. Multiplying these BAFs by the GLI WC of 1300 pg Hg/L yields total mercury concentrations in fish of 0.108 $\mu\text{g Hg/g}$ and 0.451 $\mu\text{g Hg/g}$ for trophic levels 3 and 4, respectively. Both values are slightly (1.3 times) higher than those calculated using the WV_f in the Report to Congress.

UNCERTAINTY ANALYSIS

A probabilistic assessment of uncertainty in WV derived in the GLI and the Report to Congress cannot presently be conducted because published data are inadequate to specify distributions and correlations for most of the input variables. In particular, the data used to estimate TDs and UFs are only sufficient to generate point estimates. Moreover, while theoretically possible, a full uncertainty analysis may be of limited value since the goal of both efforts was to protect that subset of each species that feeds extensively at the top of aquatic food chains. Thus, incorporation of data reflecting the full range of dietary items upon which bald eagles feed would generate an extremely broad range of WV for this species. The authors of the Report suggested that a restricted uncertainty analysis involving distributions for each of the BAF estimates could be accomplished using existing data. They did not, however, perform this analysis.

SENSITIVITY ANALYSIS

In a sensitivity analysis, an attempt is made to characterize the extent to which a value changes with changes in the parameters upon which its calculation depends. An examination of the equation used to calculate WV suggests that a proportional relationship exists between the WV and the TD, UF, or Wt_A . The relationships between the WV and parameters that appear in the denominator are not as apparent and must be explored by varying these parameters individually in systematic fashion. For example,

with the otter and eagle, FD_3 and FD_4 tend to vary in a reciprocal manner, although in the eagle these values do not add up to 1. For the mink, FD_3 is assigned a value less than 1 and the remainder of the diet is assumed to consist of prey that are not aquatic in origin and do not contain mercury. Despite this complexity, general conclusions can be reached regarding the sensitivity of WV estimates to changes in these parameters. These conclusions can be described as follows:

- W_A can be ignored as it is quantitatively insignificant when compared to the sum of the other terms in the denominator.
- Changes in F_A will result in proportional changes in the WV .
- The WV for any species consuming only trophic level 3 fish will vary proportionally with BAF_3 .
- To some extent, changes in BAF_4 will be paralleled by changes in BAF_3 , since they are linked in any given system by a predator-prey factor (i.e., $BAF_4 = BAF_3 \times FCM_{3-4}$). A review of the literature suggests that the median value of FCM_{3-4} is about 5.0 (U.S. EPA, 1997, Vol. III, App. D).
- Accepting the exposure factors given in Table 2, WV_s for the otter and eagle will be somewhat more sensitive to changes in BAF_4 than in BAF_3 . The relative impact of a change in BAF_4 is determined, however, by the assigned values of FD_3 and FD_4 . For both the otter and eagle, FD_3 is about four times larger than FD_4 . The relative impact of BAF_4 is therefore approximately 1.25 times (5_4 divided by 4) that of BAF_3 .
- An increase in FD_4 for either the otter or eagle would result in a further increase in the sensitivity of the WV_s to changes in BAF_4 .

SCIENTIFIC UNCERTAINTIES ASSOCIATED WITH WILDLIFE VALUES FOR MERCURY

Owing to the complexity of natural systems, uncertainties associated with the derivation of WV for mercury are to be expected. Additional uncertainties derive from the relative scarcity of wildlife toxicity testing information and the need to relate individual-based effects to higher levels of biological organization (in this case, populations). Scientific uncertainties associated with the WV methodology have been reviewed elsewhere (U.S. EPA, 1995c; Abt Associates, 1995). The intent of the following discussion is to focus on areas that are especially pertinent to mercury.

Limitations of the Toxicity Database

Substantial uncertainties underlie most of the wildlife toxicology data for mercury. Comparisons of NOAELs and LOAELs among species require the adoption of unproven assumptions about the uptake, distribution, elimination, and toxic effects of mercury. Conclusions based upon extrapolation from one species to another are, therefore, tenuous. Additional uncertainties arise when extrapolating from LOAELs to NOAELs, and from

subchronic endpoints to chronic endpoints. In some instances there may also be a need to account for the possibility that test results do not adequately protect the most sensitive individuals. This may be particularly important for protected species, where there is a concern for individual animals.

Toxicity studies utilizing “naturally incorporated” mercury (e.g., in contaminated fish) are complicated by the possibility that mercury is accompanied by other contaminants, which may exert some or all of the observed effects. Ideally, it is desirable to compare the effects of mercury that has been incorporated naturally with effects due to mercury that has been spiked into a prepared diet. By spiking mercury into the diet, the researcher can better control the dose to the animal. The possibility exists that mercury bioavailability from different diets varies. However, the toxicity and bioavailability of methylmercury to cats were similar regardless of whether it was given in contaminated fish or spiked into the diet (Albanus et al., 1972; Charbonneau et al., 1976). As indicated previously, the oral bioavailability of methylmercury in higher vertebrates tends to be very high.

It is not possible to test all wildlife species of interest. The use of uncertainty factors for species extrapolation is likely, therefore, to continue. Nevertheless, existing information can be used to suggest which species should be singled out for consideration. Criteria used to select the species evaluated in the GLI were given previously. Additional criteria can be envisioned, particularly for site-specific applications. The WV methodology also provides that where appropriate, toxicokinetic and toxicodynamic considerations may be used to adjust TD levels. An example is provided in the Report to Congress, wherein a decision was made not to adjust the TD for avian species downward using a species-to-species uncertainty factor (i.e., $UF_A = 1$). This decision was based upon accumulating evidence that suggests that piscivorous birds and mammals have evolved the capability to demethylate some of the methylmercury to which they are exposed. On this basis it was concluded that mallard ducks (an omnivorous species) are likely to be more sensitive to methylmercury than the piscivorous species these calculations were designed to protect. The GLI did not explicitly consider the possible importance of toxicokinetic differences between bird species. It was, however, noted that among tested species, mallard ducks appear to be more sensitive to methylmercury than most birds. This observation was then used to justify a relatively low UF_A of 3 when adjusting the TD for mallards.

Finally, efforts to compare NOAELs for different wildlife species (or with human NOAELs) are complicated by differences in the ability of a given study to reveal an adverse effect when it occurs. For wildlife, most of the toxicity endpoints evaluated to date can be considered severe adverse effects. Very few studies have been designed to investigate subtle behavioral effects that would suggest an adverse impact on the central nervous system. Developmental neurotoxicity endpoints are of particular

interest because of their demonstrated sensitivity in methylmercury dosing studies with laboratory animals. Recent studies of human populations also suggest that adverse impacts of methylmercury on the developing nervous system can occur at delivered dose levels well below those that have any other discernable effect (U.S. EPA, 1997, Vol. V; Grandjean et al., 1997). The question arises, what would the LOAEL or NOAEL for a given wildlife species have been had the researcher been evaluating (or been able to detect) these more subtle effects? One possible approach to this question would be to examine the results of studies with nonwildlife species in which both severe and more subtle effects were observed and determine the corresponding difference between dose levels. The question remains, however, whether these more subtle effects are relevant to a process (WV derivation) that is ultimately intended to protect populations (see later subsection, Individuals Versus Populations).

In their reviews of toxicity studies with wildlife, the authors of both the GLI and the Report to Congress attempted to identify NOAELs for use as the TD in the WV algorithm. It has been argued that NOAELs are unnecessarily conservative and should not be used to set WV. Suggested alternatives include the calculation of a "threshold" dose as the geometric mean of the LOAEL and NOAEL, or a benchmark dose procedure in which safety factors are applied to a characterized level of effect (e.g., division of an ED₁₀, the dose that affects 10% of the study population, by a factor of 10). Unfortunately, existing toxicity data for mercury in wildlife are insufficient to employ a benchmark dose approach. Moreover, as indicated previously, there is serious concern about whether current toxicity testing methods are capable of detecting real, adverse effects on wildlife species.

Toxicity studies with mallard ducks (Heinz, 1974, 1975, 1976a, 1976b, 1979) were used in both the GLI and Report to Congress to calculate the RfD for avian species. These studies did not, however, yield a NOAEL. The data were therefore examined to identify a LOAEL, which was then adjusted using a UF_L. In the GLI, chronic studies with avian and mammalian wildlife species were evaluated for the purpose of guiding the specification of UF_L values (U.S. EPA, 1995c; Abt Associates, 1995). Although limited to just five chemicals (cadmium, DDT, DDE, dieldrin, and mercury), this data set was sufficient to calculate 275 LOAEL-to-NOAEL ratios. Ninety-seven percent of these ratios were less than or equal to 10, and 50% were less than or equal to 3. Based upon the results of this analysis, it was recommended, with appropriate qualification, that a range of 1–10 be used to set the UF_L values employed in the GLI.

A similar analysis was conducted in the Report to Congress, but was limited to an evaluation of toxicity studies with methylmercury. Nineteen studies were identified for this purpose. Selection criteria included (1) nonhuman mammals as test subjects, (2) oral exposure (with preference given to dosing in food or drinking water), and (3) chronic or subchronic

exposure durations (with exceptions for reproductive and developmental toxicity where such distinctions are less relevant). Endpoints used in this analysis included lethality, neurotoxicity, renal toxicity, gastrointestinal toxicity, immunotoxicity, developmental toxicity, and reproductive toxicity. In all, 20 LOAEL-to-NOAEL ratios were calculated. Only one ratio was greater than 10, and most were between 1 and 2 ($n = 6$), or 4 and 5 ($n = 9$).

Both of these analyses were patterned after an earlier study by Dourson and Stara (1983), in which LOAEL-to-NOAEL ratios were developed from chronic and subchronic dosing studies with rats (Weil & McCollister, 1963). Altogether, 52 ratios were calculated using data for 33 different compounds. None of the ratios exceeded 10, and 96% were 5 or less. The most appropriate interpretation of the ratios developed in all three efforts is that the threshold for toxic effects, defined by each study, lies within the bounds of the experimentally derived LOAEL divided by a UF_L , and that most of the effects thresholds are encompassed by using a UF_L of 10 or less. Dourson and Stara (1983) recommended the application of a relatively large UF_L when estimating a NOAEL from an unbounded LOAEL for a severe toxicological effect. Conversely, a low UF_L was recommended when the toxicological effect is considered to be relatively mild. Similar guidance was given in supporting documents for the GLI (U.S. EPA, 1995c; Abt Associates, 1995).

Questions remain, however, concerning the utility of this approach for setting UF_L in WV derivation efforts. In particular, the distribution of LOAEL-to-NOAEL ratios tends to reflect the dose spacing selected for experiments of this type. This is particularly problematic when the number of applicable studies is small. An examination of the wildlife toxicity database also suggests that the dose spacing used in these studies is often larger than that employed in comparable studies with laboratory animals (U.S. EPA, 1995c; Abt Associates, 1995). Lacking the data needed to do so, the authors of the GLI and the Report to Congress did not segregate ratios by toxic endpoints. It is difficult, therefore, to assess the "steepness" of the dose-response curve for any given effect, or to compare the magnitude of a response observed in any particular study with that seen in the study used to estimate the RfD (e.g., reproductive effects on mallard ducks).

Validity of BCF/BAF Paradigm

BAFs used to derive a WC for mercury in the GLI were calculated using experimentally determined BCF values for fish. This approach was based on a bioaccumulation paradigm ($BCF \times$ food chain multiplier) that was originally developed to describe the accumulation of persistent hydrophobic organic compounds in aquatic organisms. The approach assumes that the BCF determined in the laboratory represents a near steady-state condition. In the absence of metabolic biotransformation, rapid growth, and other potentially complicating factors, the chemical concentration achieved by the organism should then reflect an equilibrium distribution between it and the exposure water.

Field studies indicate, however, that many fish accumulate mercury throughout their lives, often in a nearly linear fashion with age (Scott & Armstrong, 1972; MacCrimmon et al., 1983; Wren et al., 1983; Mathers & Johansen, 1985; Skurdal et al., 1985; Wren & MacCrimmon, 1986; Sorensen et al., 1990; Jackson, 1991; Gutenmann et al., 1992; Lange et al., 1993). There are probably several reasons for this, including the sequestration of covalently bound methylmercury in tissue, thereby maintaining a concentration gradient for continued uptake, and the fact that most of the mercury accumulated by fish is taken up from dietary sources. Thus, particularly for long-lived piscivorous fish, a relatively short (1 yr or less) waterborne exposure is likely to underestimate the extent of accumulation that takes place in nature. As indicated previously, BAFs given in the Report to Congress were calculated from measured methylmercury concentrations in fish and water. Statistical distributions developed from these data are characterized by considerable variability. Part of this variability is due to the continuing accumulation of methylmercury in fish taken to represent trophic levels 3 and 4. Presently, however, it is not possible to separate this from other potential sources of variability in field-derived BAFs.

Variability in BAFs Within and Among Aquatic Systems

The utility of the BAF concept derives from the fact that for compounds that bioaccumulate, chemical concentrations in water and aquatic biota tend to be highly correlated. In theory, therefore, an increase in aqueous chemical concentration will result in a proportional increase in tissue residues, provided that there is sufficient time for the system to respond to this change and that nonlinear kinetic processes do not control accumulation. Upon closer examination, however, it can be seen that the strength of this correlation depends on the data taken to represent each of the input values. In the Report to Congress, dissolved methylmercury was considered to be the best estimator of mercury bioaccumulation potential in a given water body. Speciation data from natural systems suggest that most of the methylmercury in water exists in a dissolved form. Questions remain, however, concerning the bioavailability of methylmercury that is bound to dissolved organic carbon. Future refinement of the BAF approach may require the development of methods to identify the "freely dissolved" (i.e., diffusible) fraction of methylmercury. This approach is now being used in BAF calculations with high $\log K_{ow}$ organic compounds to account for differences in bioavailability among systems (Burkhard et al., 1997).

Uncertainty in BAF estimates was quantified in the Report to Congress using a Monte Carlo simulation technique (U.S. EPA 1997, Vol. III, App. D). The advantage of this approach is that it explicitly includes known variation, thereby providing for the statistical possibility of a high or low end result. In addition, the distributions themselves follow from the processes at work. For example, a skewed BAF distribution for trophic level 4 would be expected from random sampling of a fish population due to the relative

scarcity of the oldest individuals. Based upon a survey of published data, the distribution of methylmercury values as a percent of total in water also appears to be highly skewed. As more information about mercury is obtained, these distributions can be improved.

Other potential sources of variability in BAF values are less well known. Included among these are spatial and temporal variation in methylmercury concentration within systems, and the responses of exposed animals to these changes. Although the geometric mean of measured BAFs for a given system is an appropriate metric for calculating a mercury WV, the amount of within-system variability has important implications for assessing the risk to wildlife that inhabit the system. In recent years, environmental sampling efforts have emphasized improvements in measurement quality, including reductions in sample contamination and the quantitation of individual mercury species. An effort has also been made to correlate measured accumulation in aquatic biota with attributes of different systems in an effort to better understand variation among lakes. Future efforts should also be directed toward understanding the extent and underlying basis of within-lake variation in mercury BAFs. Of particular importance is the question whether sources of within-lake variation bias the central tendency (i.e., the mean BAF for the system at each trophic level) in current sampling designs.

Finally, it is important to consider the possibility of regional bias. Most of the speciation data collected to date have been obtained from oligotrophic systems in the northern tier of states. It has been argued that BAFs based on regression data for a large number of lakes should be given greater weight (perhaps in proportion to the number of lakes sampled) than data from a single location. This, however, would increase the degree of regional bias that is already present in the analysis.

Selection of Species of Concern

The wildlife species taken to represent piscivorous birds and mammals in the GII and the Report to Congress were selected on the basis of their suspected exposure and not because of their inherent sensitivity to mercury. Lacking the necessary toxicity information, little guidance is available concerning which wildlife species are most sensitive to mercury. In addition, there may be problems associated with comparisons of laboratory and field data. For example, laboratory data suggest that mercury residues in eggs exceeding 0.5 $\mu\text{g/g}$ are associated with impaired reproduction in mallard ducks (Heinz, 1974, 1976a, 1976b, 1979) and ring-necked pheasants (Fimreite, 1971). In contrast, reproduction in herring gulls appeared to be unaffected even when egg residues exceeded 10 $\mu\text{g/g}$ (Vermeer et al., 1973). Taken alone, these data suggest that mallards and pheasants are more sensitive to the toxic effects of mercury than are gulls. This may in fact be true; however, such comparisons are complicated by the presence/absence of additional factors such as confinement, handling, weather, differences between natural and prepared diets, the possible ameliorative effect of

dietary selenium, and the interplay between “inherited” (egg) mercury and mercury that the chick consumes. Finally, toxicity can be difficult to observe in a field study, even when it is occurring. In 18 of 38 nests under study by Vermeer et al. (1973), hatching success could not be evaluated due to nest predation or some other type of disturbance.

Exposure and sensitivity must be considered together. For example, if a species was five times more sensitive than the eagle on a delivered dose basis, but because of its dietary habits received a much smaller dose, it might not exhibit adverse effects at mercury concentrations in water that are harmful to the eagle. Toxicokinetic considerations may also be important. It is well known that birds eliminate a substantial amount of mercury through incorporation into plumage (Braune & Gaskin, 1987). The frequency and extent to which birds moult may therefore impact their apparent sensitivity in an environmental setting. Finally, as discussed previously, most if not all wildlife possess some capability to detoxify methylmercury. Enhanced demethylation would be particularly important if it represented an adaptive strategy for piscivorous species.

There is also a need to consider animals other than birds and mammals. In particular, there is a need to characterize the exposure of carnivorous reptiles such as the snapping turtle and American alligator, which consume large quantities of fish. The alligator is also known to feed on animals (e.g., wading birds) that prey upon aquatic biota.

Wildlife Feeding Habits

The dietary preferences of the wildlife species identified in the Report to Congress are shown in Table 2. Similar assignments appear in the GLI. The rationale behind these assignments can be found in two recent U.S. EPA publications that were developed for the purpose of supporting WV calculations (U.S. EPA, 1993c, 1995c). For some species, such as the kingfisher and river otter, it is reasonable to assume that fish always comprise a high percentage of the diet. For others, such as the eagle and mink, considerable variations in diet exist (U.S. EPA, 1993c, 1995c). For example, bald eagles living in the Great Lakes region may consume significant numbers of herring gulls (Kozie & Anderson, 1991). Since the gulls themselves are piscivores, feeding primarily at trophic level 3, it has been argued that when an eagle consumes a gull it is feeding at trophic level 4 or higher (the gull:forage fish mercury concentration ratio generally exceeds the ratio of mercury concentrations at trophic levels 3 and 4). Eagles living in other parts of the country may consume relatively few fish, feeding instead on carrion, including rabbits, squirrels, and dead domestic livestock such as pigs and chickens (Harper et al., 1988; U.S. EPA, 1995e). Finally, natural exposures vary in both spatial and temporal domains. This is particularly true of species that migrate, including the bald eagle, osprey, loon, and belted kingfisher. The need to incorporate this type of information and the means by which this can be accomplished remain open questions.

Variability in BAFs at Each Trophic Level

A concern related to the issue of feeding preference is the possibility that trophic levels presently assigned to selected wildlife species overestimate the true extent to which they are exposed to mercury. This is because BAFs are developed to represent the average value for a trophic level, when in fact piscivorous birds and mammals may be more likely to target prey at the lower end of the size (age) distribution. Thus, eagles are more likely to consume a 1-kg northern pike than a 10-kg individual, yet both are represented in the BAF for trophic level 4. Similarly, kingfishers are probably limited to smaller individuals of trophic level 3 than would be true of an osprey. A possible approach to this problem is to use Monte Carlo techniques to analyze individual field data sets. Specifically, it would be of interest to determine whether percentile information from the generated distributions can be related to fish of known size. It may then be possible to use these data to calculate BAF estimates that would have greater applicability to a selected wildlife species or site.

Species Versus Taxa

The mercury WV_i derived in the GLI and the Report to Congress were driven, respectively, by intermediate calculations for birds and mammals. The WV_i for avian species was calculated in turn as the geometric mean of WV_s for three (GLI) or four (Report) species. In both efforts the WV_i for mammals was calculated as the geometric mean of WV_s for two species. This approach is reasonable if the WV_s calculated for each species within a taxa are similar, but would fail to protect species for which the WV_s is much lower than the others with which it was averaged. In the Report to Congress, WV_s calculated for eagle, osprey, loon, and kingfisher were all within a factor of 3 of one another. WV_s for mink and otter agreed to within a factor of about 1½. An examination of WV_s in the GLI reveals similar levels of agreement within taxa. As additional data are gathered, it may be necessary to identify species that, by virtue of sensitivity and/or exposure, are particularly vulnerable to mercury. Decisions could then be made concerning the advisability of special measures to ensure their protection.

Individuals Versus Populations

The methods used to develop WV are based on effects data from studies of individual animals, while the stated assessment endpoint is the maintenance of wildlife populations. The relationship between individuals and populations undoubtedly varies among species, and perhaps among different geographical regions for the same species. For some populations, the loss of a substantial number of individuals may have little effect, particularly if environmental factors limit population size (i.e., carrying capacity). Animals that are capable of dispersing over large areas present additional complications. For example, negative impacts occur-

ring within a given location may be difficult to observe due to a continuous influx of as yet unaffected individuals. For other populations, in particular those with low fecundity and a limited ability to disperse, loss of a relatively few individuals could have a large impact. A focus on populations may not always be appropriate, particularly when endangered species are involved. The same may also be true if various factors result in adverse regional impacts. For example, although 90% of a species nationwide might be protected by a WV for mercury, mortality within a given region could be high if attributes of lakes and rivers in that area contributed to higher than average accumulation of mercury in the aquatic food chain. Alternatively, there is a potential for indirect effects on populations due to changes occurring at the community level of biological organization. Thus, an adverse impact on one population could have a large effect on the animals upon which this population preys. In this case, the focus on extrapolating adverse effects from individuals to populations may be too restrictive.

SUMMARY

The procedure used to derive WV is relatively recent in origin, and it is likely that with the accumulation of newer data and models it will be modified and refined. The first WV for mercury were published in 1995 as part of the GLI. These WV were used to calculate a WC for mercury in the Great Lakes basin. Calculated as total mercury in unfiltered water, the value of this criterion is 1300 pg Hg/L. A second attempt to derive WV for mercury was published in 1997 as part of a Congressionally mandated report on airborne mercury emissions. The authors of the Report to Congress based their analysis on published mercury speciation data for aquatic ecosystems. Although limited, these data were believed to be sufficient to estimate BAFs for methylmercury from measured concentrations in fish and water, and to calculate WV on a methylmercury basis. Calculated as methylmercury in filtered water, the WV_f in the Report is 50 pg Hg/L. A direct comparison of the WC given in the GLI and the WV_f derived in the Report to Congress requires that assumptions be made concerning the speciation of mercury in natural water. Adopting these assumptions, it can be shown that the WV_f for methylmercury in the Report corresponds to a total mercury WV_f of 910 pg Hg/L (total in unfiltered water).

WV are designed to protect wildlife populations from adverse impacts associated with the ingestion of contaminated surface waters or aquatic life taken from these surface waters. The derivation of a WV does not by itself constitute an ecological risk assessment. A WV can be used, however, to provide for a simple assessment of risk at a given site by determining whether the aqueous concentration of a particular contaminant exceeds the derived value. This approach is similar to the well-known hazard quotient method and employs the same type of exposure and effects point estimates.

Alternatively, it is possible to compare mercury residues in fish corresponding to a WV_f with concentrations measured in field-collected animals. Previously, it was shown that the WV_f in the Report to Congress corresponds to methylmercury concentrations of 0.077 and 0.346 $\mu\text{g/g}$ at trophic levels 3 and 4. Based upon an analysis of two national-scale fish sampling efforts, the authors of the Report to Congress calculated “national average” total mercury concentrations in fish (U.S. EPA, 1997, Vol. VI). Respectively, the calculated values for trophic levels 3 and 4 were 0.052 and 0.26 $\mu\text{g Hg/g}$, most of which is thought to exist as methylmercury. Mercury concentrations in fish considerably higher than those corresponding to the WV_f in the Report have been noted, however, in several locations. It should also be emphasized that the WV_f given in the Report was calculated using geometric mean BAF values. By definition, therefore, BAFs for trophic levels 3 and 4 were higher than mean values in approximately half of the systems for which field data were available.

Existing effects data for wildlife species yielded similar RfDs for birds and mammals in both the GLI and the Report to Congress. In performing these calculations, the authors of both efforts used very few uncertainty factors, and the uncertainty factor values were small. Previously, Barr (1986) reported that 0.3 $\mu\text{g Hg/g}$ in trophic level 3 fish caused adverse effects on reproduction in a population of wild loons. The difference between demonstrated effect (0.3 $\mu\text{g Hg/g}$) and derived no-effect (0.077 $\mu\text{g Hg/g}$) residues in fish may therefore be less than a factor of 4. Hazard quotients derived previously for great egret (Jurczek, 1993; Sundlof et al., 1994) and mink (Giesey et al., 1994) ranged from 1.2 to 6.6. These calculations suggested the possibility of local impacts on these two species. Based on these and other similar studies, the authors of the Report to Congress concluded it is likely that individuals of some highly exposed populations of birds and mammals are consuming fish at or very near adverse effect levels.

Variability in BAFs within and among water bodies contributes to substantial uncertainty in the derivation and use of WV_f for mercury. In the Report to Congress, the 90% confidence interval for the trophic level 4 BAF (field-derived, methylmercury basis) encompasses a 4.4-fold range of values (Table 1). Most of this variability is thought to reflect real variation in mercury bioaccumulation and biomagnification within and among aquatic systems. Accordingly, it does not make sense to label the correlation between mercury levels in fish and water “good” or “bad.” Instead, it is a risk manager’s responsibility to consider this variability when evaluating the potential consequences of different management options.

In the last several years, considerable progress has been made in understanding and predicting how chemical and biological factors affect mercury bioaccumulation in aquatic biota, and in time it may be possible to adjust BAF predictions as needed to represent specific surface waters of concern. The prospect for continuing uncertainty surrounding these estimates argues for adoption of a residue-based approach—that is, the use of mea-

sured mercury residues to characterize bioaccumulation in aquatic biota at a specific site. The continued use of water-quality guidelines in the context of setting wastewater discharge limits, developing total maximum daily loadings (TMDLs), and evaluating site remediation efforts requires, however, that "safe" values be established for mercury concentrations in water. Clearly, there is a need for models and methods that would allow risk assessors to predict tissue residues in wildlife from mercury concentrations in water and vice versa, so that data from all sources can be interpreted and used.

Research to improve the derivation of WV for mercury should be focused on the collection of chronic toxicity information for piscivorous wildlife species, using endpoints relevant to the mode of action of methylmercury, including assessments of both reproductive and behavioral effects. These efforts should be coordinated with research to determine whether and to what extent impacts on piscivorous wildlife species are occurring, and the effects that local-scale impacts may have on widely distributed populations. Additional work is needed to better understand the variation in BAF distributions and to improve existing techniques for incorporating these data into WV derivation efforts.

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