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Use of Traditional Foods in a Healthy Diet in Alaska: Risks in Perspective

Second Edition:
Volume 2. Mercury

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Risks in Perspective

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Executive Summary

Mercury occurs naturally in the earth's crust, is ubiquitous in the environment, and is a component of freshwater and marine fish and mammals. Human industrial activities such as coal burning contribute to the global distribution of mercury in the environment. Global mercury emissions have increased since the 1700s. Currently, known man-made emissions of mercury roughly equal known natural emissions. Mercury has many chemical forms that occur naturally in the environment. From a public health standpoint, methyl-mercury is the most important.

Alaskans are exposed to methylmercury primarily from ingestion of fish and marine mammals. Methylmercury concentrations in the most frequently consumed fish (e.g., salmon, cod, halibut, pollock, sole, and herring) are very low, consistently below 0.2 μg/g [parts per million, ppm, wet weight (all tissue concentrations are wet weight unless noted otherwise)]. This is one-fifth of the Food and Drug Administration (FDA) action level for commercial sale of seafood of 1 ppm. Alaska salmon average 0.05 ppm of methylmercury. Similarly for marine mammals, except for some beluga whale tissues, average methylmercury concentrations are below 0.2 ppm. Bowhead whale tissues (e.g., muscle, blubber, epidermis, liver and kidney) contain very low methylmercury concentrations (<0.02 ppm). Older fish and marine mammals that are higher on the food chain have higher concentrations of methylmercury.

Currently, there is scientific and public health agreement regarding safe levels of dietary methylmercury intake for adults. The World Health Organization (WHO) developed guidelines based upon the Minimata and Niigata, Japan poisoning outbreaks associated with heavily industrial methylmercury-polluted fish, and on an Iraqi mercury-poisoning outbreak, where grain treated with a mercury-containing fungicide intended for crops was instead used to bake bread. The WHO relied heavily upon data from these tragedies to develop a provisional tolerable weekly intake (PTWI) for methylmercury of 230 μg, and for total mercury of 300 μg. This weekly intake corresponds to a daily dose of 0.5 μg/kg/day.

Scientists, medical, and public health professionals do not agree on safe levels of dietary intake of methyl-mercury to protect the developing fetus. Two large-scale, rigorous, epidemiologic studies were designed to to determine if subtle neurodevelopmental effects could be associated with chronic low-level *in utero* exposures. One study was conducted in the Faroe Islands; the other was conducted in the Seychelles Islands. These studies produced different results.

In the Faroe Islands study, no clinical or neuro-physiological methylmercury-related abnormalities were noted in 917 children evaluated at 7 years of age. However, subtle decreases in some neurodevelopmental test results were found to be associated with low-level mercury exposure, although most test scores of highly exposed children were normal. The median maternal hair mercury concentration was 4.5 ppm. Methylmercury exposure in this cohort occurred primarily through the consumption of pilot whale meat (1-2 meals a week; average methylmercury concentration detected in pilot whale meat was 1.6 ppm) which also contained polychlorinated biphenyls (PCBs). PCBs are suspected to cause similar subtle neurodevelopmental effects. Therefore, in this cohort, it is not possible to separate the contributions of PCBs and methylmercury, or their potential interaction, to the subtle decreases noted in the neurodevelopmental tests. Nevertheless, the U.S. Environmental Protection Agency (USEPA) chose to base its recommendations for dietary exposure primarily upon the data from the Faroe Islands study.

In the Seychelles Islands study no neurodevelopmental effects were detected in 643 children. The median maternal hair mercury concentration was 6.6 ppm, an exposure higher than the Faroe Islands. Over 75% of the mothers reported eating 10-14 fish meals per week. Average fish concentrations of methylmercury were approximately 0.3 ppm. In contrast to the Faroe Islands study, exposure to PCBs or other potential neurotoxins were extremely low in the Seychelles Islands.

In 2001, the USEPA developed a new reference dose (RfD) (the safe dose that can be consumed every day over a lifetime of 70 years without any ill effects), relying on the Faroe Islands study, for methylmercury that is 0.1 μg/kg/day. In developing their new RfD, the USEPA made a decision to dismiss the results of the Seychelles Islands study. The EPA also made a decision not to take into account the well-known health benefits of fish consumption or to assess the risks associated with loss of nutrients from the diet.

In 2001, the USEPA and FDA issued generic national fish consumption advisories recommending pregnant women, those who could become pregnant, nursing mothers, and young children to restrict consumption of recreationally caught fish to 6 ounces per week (USEPA) and commercially caught fish to 12 ounces per week (FDA). Because extensive data existed to document that many species of fish have methylmercury concentrations far below 0.2 μg/g (ppm), the average level upon which these severe dietary restrictions were based, the FDA amended the 2001 fish advisory to include the following:

> "Some kinds of fish that are known to have much lower than average levels of methylmercury can be safely eaten more frequently and in larger amounts. Contact your federal, state, or local health or food safety authority for specific consumption recommendations about fish caught or sold in your local area."

In 2001, the Alaska Division of Public Health (ADPH) convened an advisory group of public health officials, research scientists, and Native health leaders to review all available information concerning mercury exposure in Alaska. Based upon consensus, the Alaska Division of Public Health strongly recommended that all Alaskans, including pregnant women, women who are breast-feeding, women of childbearing age, and young children continue unrestricted consumption of fish and marine mammals from Alaskan waters as part of a balanced diet.

Because of the heavy consumption of fish and marine mammals in Alaska, several initiatives were begun to increase fish and human biomonitoring.

The Alaska Department of Environmental Conservation implemented a statewide fish-monitoring program. The average concentration of methylmercury in the most frequently consumed fish in Alaska (five species of Pacific salmon) is very low (<0.05 ppm). Recent human biomonitoring studies in Alaska have documented that levels of methylmercury exposure are well below levels associated with known adverse health effects. Results from the Alaska Division of Public Health's Statewide Maternal Hair Mercury Biomonitoring Program are well below the World Health Organization's No Observed Effect Level of 14 ppm in hair. The median and mean hair mercury concentrations for pregnant women (n = 176) were 0.47 ppm and 0.71 ppm (range 0.02 – 6.35 ppm). The median and mean hair mercury concentrations for women of childbearing age (n = 60) were 0.63 ppm and 1.2 ppm (range 0.15 – 8.36 ppm). In addition, results from the Alaska Native Tribal Health Consortium's infant-maternal cord-blood study were also well below the WHO No Observed Effect Level of 56 ppb in blood. The average total mercury concentration for the Barrow area (n = 29) was 1.5 ppb (range = not detected - 4.5 ppb) and 6.5 ppb (range = 0.6 ppb – 21 ppb) for the Bethel area (n = 52).

Public health officials from the international Arctic Monitoring and Assessment Programme have monitored the impacts of arctic contaminants on human health since 1991. They concluded that the nutritional and physiological benefits of traditional arctic diets outweigh potential risks from exposure to contaminants in most areas of the Arctic, and advised local public health policy makers to encourage continued traditional food use when indicated by risk-benefit analyses.

National fish advisories are based solely upon risk assessment -- they do not consider the well-established public health benefits of fish consumption. Evaluation of food safety and the development of food consumption advice should occur within a multidisciplinary public health framework. Fish is a healthy and readily available food item that is high in protein, low in saturated fat, and a rich source of omega-3 fatty acids and antioxidants such as selenium and vitamin E. Limiting the consumption of fish or marine mammals will reduce significant health benefits, causing unintended negative health consequences.

The Alaska Division of Public Health continues to recommend that all Alaskans, including pregnant women, women who are breast feeding, women of childbearing age, and young children continue unrestricted consumption of fish and marine mammals from Alaskan waters as part of a balanced diet. The ADPH is continuing efforts to expand human biomonitoring for methylmercury and persistent organic pollutants to monitor trends and provide evidence to support dietary recommendations.

Introduction

Since the last draft of this document (ADPH 1998), the Alaska Division of Public Health and its collaborating partners have continued to monitor evolving evidence regarding the safety and potential risks of Alaska seafood containing methylmercury. Public concerns and unwarranted anxiety have been increased by broad-based national fish advisories. To address these concerns and update dietary guidelines for Alaskans, the Alaska Division of Public Health (ADPH) reviewed the current toxicologic, epidemiologic, and risk assessment literature on methylmercury, human biomonitoring data, and the known benefits of seafood consumption.

Background

Mercury has several forms that occur naturally in the abiotic and biotic environment. The most common forms are metallic mercury (Hg^o), inorganic salts such as mercury chloride ($HgCl_2$), mercury sulfide (HgS), and organic mercury in the form of methylmercury (CH_3Hg^+). Alaskans are primarily exposed to mercury through fish and marine mammal consumption. Methylmercury is the form of greatest public health concern. Topics covered in this chapter include basic chemistry and environmental concentrations, potential health effects, potential biochemical mechanisms, risk assessment/food consumption guidelines, dietary intake estimates, human exposure studies, Alaska's public health advice, and recommendations for further action.

Mercury in the Environment

Mercury (Hg) is an element that occurs naturally in the earth's crust and is ubiquitous in the environment. All classes of rocks contain some amount of mercury ore, but the mineral cinnabar contains the greatest concentration, 86.2% mercury (Stokinger 1981). There are many forms of mercury in the environment. Metallic (elemental) mercury is a shiny, silver-colored liquid at room temperature such as used in thermometers. Mercury is refined from HgS ore found in cinnabar mines and is used in a variety of products such as thermometers, batteries, electrical switches, and in the production of chlorine gas and caustic soda (ATSDR 1999). Most inorganic mercury salts are white powders or crystals (e.g., $HgCl_2$ and Hg_2Cl_2). HgS is brick red or black in color. Methylmercury is formed naturally through methylation of Hg^{2+} by microorganisms in sediments and soils.

Mercury is dispersed naturally throughout the environment through weathering processes, erosion, volcanic emissions, and off-gassing of the earth's crust. Among human activities that release mercury into the environment, coal burning, mining and smelting of mercury ores, and industrial emissions from factories using mercury in production processes are most responsible. Incineration of garbage, including medical, agricultural and municipal wastes also release mercury into the environment (ATSDR 1999).

Figure 1 is a schematic of mercury cycling in the aquatic environment (adapted from NRC 2000). Global bio-geochemical cycling of mercury consists of emission, deposition, and revolatilization of the various forms of mercury. The most significant input of mercury to the environment is from air emissions. Once released to the atmosphere, mercury may be deposited to the surface in the form of Hg^{2+} or transported great distances in the form of elemental mercury (Hg^o). Global transport/residence times of Hg^o can be 6 days to 2 years (ATSDR 1999). Mercury emitted into the atmosphere at lower latitudes can be transported and deposited in the Arctic. In the atmosphere, elemental mercury is oxidized to other forms of mercury such as Hg^{2+} that can bind to particles that are removed from the atmosphere by wet or dry deposition. Once Hg^{2+} enters the aquatic environment, it may be converted to methylmercury via microorganisms in fresh and salt water and sediments. Once mercury is methylated, it may accumulate in biota and concentrate up the food chain as smaller fish are consumed by larger fish. The highest concentrations of methylmercury are found in animals at the top of the food chain such as larger older piscivorous fish, carnivorous marine mammals, or piscivorous birds. In sediments, Hg2+ is also converted to insoluble HgS.

On a worldwide basis, approximately 5000 metric tons of mercury are emitted to the atmosphere each year. Anthropogenic inputs equal or slightly exceed natural emissions (USEPA 1997; UNEP 2003). North America contributes about 11 percent of the total mercury emitted to the atmosphere. Asia emits roughly one-half of the global output. Coal burning in China is a major contributor (Pirrone et al. 2001). Worldwide mercury emissions have increased 2 to 9 fold since the 1700s, indicated by lake sediment cores and precipitation data (Heyvaert et al. 2000; Swain et al. 1992; Lorey and Driscoll 1999; Hermanson 1998; Meger 1986). In general, mercury concentrations in Arctic lake sediments, peat bogs, and biota have increased since the 1700s, but this temporal trend varies depending on location (AMAP 2002). One of the few studies in Alaska that examined lake sediment core data (dated c.a.1845), indicated that only a small increase in mercury deposition occurred compared to other areas in the Arctic (Landers et al. 1995).

Mercury in Humans-Historical Evidence

Archeological data of ancient human hair demonstrate past exposure (Table 1). For example, in Barrow, total mercury in hair was 4.8 ppm in a 25 year-old and 1.2 ppm in a 50-year-old mummy from the Barrow frozen family dating back to 1460 A.D. (Toribara et al. 1984). In Canada, 5th and 12th century hair methylmercury levels ranged from 0.8 ppm to 3.7 ppm with a mean level of 1.7 ppm among eight individuals (Wheatley et al. 1988). In Greenland, the mean total hair mercury level of 15th century mummies was 3.1 ppm among six adults and 10.0 ppm among 2 children (Hansen et al. 1989). The mean total mercury concentration in sixteen human hair samples from the Karluk Archeological site (1170 A.D. to 1660 A.D.) in Kodiak, Alaska was 1.33 ppm and the mean methylmercury concentration was considerably lower (0.03 ppm) (Egeland et al. 1999).

The ADPH recently analyzed ancient human hair mummies from Alaska's Aleutian Islands (Middaugh et al. 2002). After receiving permission from The Aleut Corporation, the Museum of Aleutians, and the Smithsonian Institute, ADPH analyzed hair samples from 4 infants and 4 adults that radiocarbon dating established as approximately 550 years old, dating to about 1450 A.D. The average level of methylmercury in adults was 1.2 ppm and in infants 1.4 ppm. Segmental hair analysis showed patterns of higher and lower methylmercury in centimeter segments, compatible with seasonal and event specific changes in methylmercury exposure through a subsistence fish and marine mammal diet. All of these results from ancient remains are consistent and provide evidence that humans have always been exposed to naturally occurring mercury through fish and marine mammals in their diets.

Methylmercury Concentrations in Alaskan Fish

Methylmercury is absorbed and biotransformed by fish in fresh and marine water via consumption of prey species. Because methylmercury has a long half-life in fish (about 2 years) (Stopford et al. 1975), mercury may bioaccumulate in fish tissue and may biomagnify throughout the food chain. Piscivorous fish (fish that eat other fish) have higher methylmercury concentrations than non-piscivorous fish. In fish, most of the total body mercury is found in muscle as methylmercury (Bloom 1992). Fish with higher concentrations of total mercury contain relatively higher percentages of methylmercury. For example, methylmercury contributed 100% and 92% of the total mercury concentration detected in northern pike collected from the Yukon (1.56 ppm) and Kuskokwim (0.579 ppm) rivers (Jewett et al. 2003). Methylmercury contributed 76% of the total mercury concentration (0.062 ppm) detected in salmon (chum, coho, and chinook) collected from four rivers in western Alaska (Zhang et al. 2001).

Since the majority of mercury detected in fish muscle is methylmercury, many researchers have analyzed total mercury (representing the inorganic and organic fractions) and assumed the measured concentration represented methylmercury. Figures 2-15 present methylmercury and total mercury concentrations detected in Alaska fish. All data are muscle tissue results except for the USEPA (2001) Cook Inlet data where whole body analysis was performed. In almost all instances, the concentrations of methylmercury in the most frequently consumed fish (based on harvest data, see Tables 6 and 8) from Alaska, such as salmon, cod, halibut, pollock, sole, and herring are well below the FDA action level for commercial sale of 1 ppm.

Noteworthy are the exceptionally low methylmercury levels in all salmon species. Salmon (chinook, sockeye, coho, chum, and pink) collected from Alaska waters have average methylmercury/total mercury concentrations ranging from 0.02 ppm to 0.09 ppm (Figure 2 through Figure 8a,b) (USEPA 2001; ADEC 2002; Zhang et al. 2001; Gray et al. 1996; USFW 2003; ADEC 2003). The longer-lived larger chinook salmon tend to have higher concentrations of methylmercury than other salmon species. These recent analytical results for salmon are consistent with a 1993 salmon research project that also found very low tissue levels of methylmercury, with the highest level reported as 0.06 ppm among the 16 fish tested from Alaska waters (FDA et al. 1993).

Average mercury concentrations in halibut (n = 1088) collected from the Bering Sea, Cook Inlet, Gulf of Alaska, Prince William Sound, and Southeast Alaska (Figures 2-5, 9, and 10) ranged from 0.035 ppm to 0.41 ppm (USEPA 2001; ADEC 2002; Hall et al. 1976; ADEC 2003). Halibut are piscivorous fish with long life spans. Older and larger halibut had higher concentrations of methylmercury.

Pollock is one of the largest commercial fisheries in Alaska. Sampling for pollock in Southeast Alaska (n = 6), Gulf of Alaska (n = 18), Aleutians (n = 12), and Bering Sea (n = 12) (Figures 5, 6 and 9) found low average mercury concentrations, ranging from 0.012 ppm to 0.064 ppm (ADEC 2002; 2003).

Cod (n=64) collected from Southeast Alaska, Cook Inlet, Gulf of Alaska, and Bering Sea (Figures 2, 3, 5, and 9) have average methylmercury concentrations ranging from 0.038 ppm to 0.11 ppm (ADEC 2002; 2003).

Sole has been collected in Southeast Alaska and the Aleutians (Figures 5 and 6). The average concentration in sole in Southeast Alaska was 0.03 ppm. In the Aleutians, average methylmercury concentrations of Dover sole (n = 6) was 0.045 ppm and the average concentration of yellowfin sole (n = 5) was 0.042 ppm.

Average herring methylmercury concentrations collected from Cook Inlet (n = 2) and Southeast Alaska (n = 2) samples were 0.019 ppm and 0.035 ppm, respectively.

Reflecting their age and trophic level, rockfish, lingcod, and salmon shark had the highest concentrations of mercury in Alaska marine fish reported to date (Figures 2 to 5, 9, 11, and 12). These fish are mainly harvested by sport fishermen, and average concentrations of methyl-mercury in them may approach or exceed the FDA action level for commercial sale of 1 ppm (ADEC 2002; 2003).

Besides salmon, other species harvested by subsistence and sport fishermen from inland waters that have been analyzed for methylmercury include burbot, sheefish, Dolly Varden, rainbow trout, whitefish, and grayling and

northern pike (Figure 13-15). Most methylmercury concentrations are relatively low. As expected, burbot and sheefish have higher concentrations of methylmercury than the other species due to their trophic level. The average methylmercury concentrations of arctic grayling vary from 0.034 ppm to 0.43 ppm. The highest concentrations in grayling reflect exposure to areas containing cinnabar deposits (Gray et al. 1994).

Northern pike are not harvested commercially but are caught in subsistence and sport fisheries. Northern pike are piscivorous fish and have long life spans; they contain some of the highest concentrations of methylmercury found in Alaskan freshwater fish (Figure 15). Average methylmercury concentrations in some areas approach or exceed the FDA action level of 1 ppm methylmercury. To date, northern pike have been sampled mainly in Western Alaska rivers and four National Wildlife Refuges in west-central Alaska (Jewett et al. 2003).

Jewett (2003) reviewed all the pike data from the last 15 years in Alaska and concluded that methylmercury pike concentrations have not changed over time. Depending on the location of sample collection or sample size, average methylmercury concentrations in pike vary by an order of magnitude (Figure 15). For example, a total of nine fish have been collected from the Andreafsky River (a tributary of the Yukon River); eight had concentrations greater than 1 ppm (Jewett 2003). On the other hand, studies that have collected larger numbers of pike in multiple drainages indicate methylmercury concentrations average about 0.5 ppm regionally. For example, the 1997 "lush fish" study conducted in the Yukon-Kuskokwim Delta by the Yukon-Kuskokwim Health Corporation reported northern pike (n=41) average concentrations of 0.53 ppm. In an analysis of fish from Kaiyuh Flats in West Central Alaska in 1993, methylmercury levels in 48 northern pike ranged from 0.091 ppm to 0.832 ppm, with a mean of 0.44 ppm (Headlee 1996). As expected, these studies demonstrate older/larger pike have higher concentrations of methylmercury (Jewett et al. 2003 and Headlee 1996).

Methylmercury Concentrations in Alaskan Shellfish

Methylmercury concentrations in Alaskan shellfish are very low (Table 2). Methylmercury was not detected (detection limit = 0.025 ppm) in most species tested. Average concentrations of methylmercury detected in four species of crab were less than 0.09 ppm.

Methylmercury Concentrations in Alaskan Marine Mammals

Trophic position determines methylmercury concentrations within the tissues of marine mammals. For example, baleen whales such as bowhead that filter feed zooplankton have considerably lower methylmercury exposures than toothed whales, such as beluga, that feed on species higher in the trophic level of the food chain (Table 3 and 4).

Unlike most fish, marine mammals have the ability to demethylate methylmercury. Mercury concentrations largely consist of inorganic mercury, especially in the liver and kidney (Smith et al. 1975; Born et al. 1981; Becker et al. 2000;Wagemann et al. 1998; Woshner et al. 2001a; 2001b). Because inorganic mercury is far less bioavailable than methylmercury, data on the ratio of methylmercury to total mercury and the amount of mercury in various tissues of different species are needed to assess the public health implications of consumption of tissues of marine mammal species. Some chemical forms of mercury in these tissues are not bioavailable.

Only a small percentage of the total mercury in organ tissues is methylmercury (Table 3). For example, in beluga whale, the mean liver methylmercury concentration was 7.4% (1.7 ppm) of the mean total mercury concentration (23 ppm), based on measurements from 24 animals (Woshner et al. 2001a). The mean kidney methylmercury concentration was 12% (0.59 ppm) of the mean total mercury concentration (5.0 ppm) (Woshner et al. 2001a). Similar results have been found in animals from other Arctic locations including Canada (Wagemann et al. 1998). Preliminary results in ringed and bearded seals from Alaska indicate this may be an age dependent relationship, and the organs of younger marine mammals may have a higher percentage of methylmercury compared to adults (personal communication Lara Dehn, University of Alaska-Fairbanks). Wagemann et al. (2000) recently determined a mass balance for mercury species in the liver of ringed seals collected in the western and eastern Canadian Arctic. Of the total mercury (31 ppm), only 2.5% (0.77 ppm) was methylmercury, 8.1% (2.5 ppm) other forms of organic mercury, 40% (12.4 ppm) inorganic mercury, and 53% (17 ppm) was assumed to be insoluble mercuric selenide (HgSe), the hypothesized end product of methylmercury demethylation.

The majority of mercury contained in marine mammal muscle is methylmercury (Table 3). For example, greater than 90% (1.1 ppm) of the total mercury (1.2 ppm) in beluga muscle was methylmercury (Woshner et al. 2001a). Similarly, 78% (0.07 ppm) of the total mercury (0.09 ppm) in polar bear muscle was methylmercury (Woshner et al. 2001b).

To estimate liver and kidney methylmercury concentrations in studies where only total mercury was measured, it was assumed 10% of the total mercury represents methylmercury (Table 4). Overall, the concentrations of

methylmercury in Alaskan marine mammal tissues are much lower than the FDA action level of 1 ppm. Except for liver and kidney tissues and the majority of beluga tissues, methylmercury concentrations in marine mammals are generally below 0.2 ppm (Tables 3 and 4). Bowhead whales tissues (e.g., muscle, blubber, epidermis, liver and kidney) contain very low methylmercury concentrations of <0.02 ppm (Woshner et al. 2001a).

Human Health Effects of Methylmercury

Methylmercury Poisoning

The critical target organ for methylmercury toxicosis is the central nervous system. Three scientifically studied tragic methylmercury-poisoning episodes elucidated the severe, toxic effects of methylmercury poisoning. These outbreaks with extremely high exposures to mercury resulted in death and severe, irreversible neurological damage. Milder forms of toxic effects were also noted.

In 1953, an undefined central nervous system disease was first identified in Minamata, a chemical manufacturing city in Japan. By 1959, investigators showed that the Minamata disease was associated with the intake of fish and shellfish from Minamata Bay, and that mercury was the probable cause of the outbreak (Kutsuna 1968). In 1965, another outbreak occurred associated with the consumption of fresh water fish contaminated by mercury and methylmercury compounds that were discharged by a chemical plant into the Agano River in Niigata, Japan (Kinjo et al. 1995).

Another widespread, tragic, mercury poisoning episode occurred in Iraq in the winter of 1971-1972, when over 6,000 people were hospitalized and 400 died from severe poisoning after mistakenly consuming bread baked from mercury-fungicide treated wheat grain intended for planting (Bakir et al. 1973).

General nervous system effects noted in these outbreaks included behavioral and sensory changes such as irritability and nervousness, tremors, visual and hearing impairment, and memory loss. In the Japan and Iraq episodes, the offspring exposed *in utero* to methylmercury showed greater signs of toxic effects than their mothers (Marsh et al. 1980; Marsh et al. 1981; Clarkson 1991). The high level of mercury exposure interfered with brain development, resulting in central nervous system disease ranging from severe brain damage to milder forms of developmental deficits and delays, such as delayed walking and talking (Cox et al. 1989). The most severe effects noted among those prenatally exposed were blindness, severe hearing impairment, and paralysis (Amin-Zaki et al. 1974). The most severely affected infants had extremely high blood levels [≥3,000 parts per billion (ppb)] of total mercury. Based upon 81 infant-mother pairs from Iraq, maternal hair concentrations above 70 ppm were associated with a 30% risk of abnormal findings in infants. High doses and long-term exposures to methylmercury can also damage the kidney, stomach and large intestine, sperm and male reproductive organs, and increase the number of spontaneous abortions and stillbirths.

Biochemical Mechanisms of Methylmercury Toxicity

The chemical form of mercury that is taken into the body determines the toxicity. The primary forms of mercury found in most marine mammal kidney and liver (Hg^{2+} and mercuric selenide) are relatively non-toxic, because Hg^{2+} does not easily cross cell membranes and mercuric selenide is essentially insoluble (Wagemann et al. 1998). Ethylmercury found in thimersol (a preservative formerly used in vaccines) is rapidly excreted from the body (7 to 10 days) compared to methylmercury (50 days) (Pichichero et al. 2002). Methylmercury found in fish skeletal muscle is bound to an aliphatic thiol such as cysteine (Harris et al. 2003). This form of methylmercury is less toxic than methylmercury chloride (the form typically used in laboratory experiments). Day-old zebrafish larvae can tolerate 20 times the methylmercury cysteine concentration compared to methylmercury chloride (Harris et al. 2003). Additional information is needed on the molecular mechanism of human toxicity for this specific form of mercury.

Past laboratory and animal studies determined methylmercury may produce its toxic effects through a variety of mechanisms that are too numerous to review in detail here. There does not appear to be one specific mechanism responsible for the toxicity of methylmercury (WHO 1990; Atchison and Hare 1994; Chang and Verity 1995; ATSDR 1999; NRC 2000). It is currently unclear whether the toxicity of methylmercury is caused by methylmercury, demethylated inorganic mercury (Hg^{2+}), or indirectly by the free radicals generated by the metabolism of methylmercury to inorganic mercury (NRC 2000). Both inorganic mercuric ion (Hg^{2+}) and methylmercury ($methylmercury^{+}$) show strong affinity for thiol/sulfhydryl-containing molecules (e.g., proteins, cysteine, and glutathione), and this binding underlies many of the mechanisms of mobility and toxicity of mercury in the body (Clarkson 1997).

Regardless of the form of the ultimate toxicant, there are a number of proposed mechanisms responsible for methylmercury toxicity. In brief, methylmercury increases oxidative stress (Zalups and Lash 1994); inhibits protein synthesis in target nerve cells (Yoshino et al. 1966; Syversen 1982); interferes with myelin (Ganser et al. 1985) and mitochondrial DNA synthesis (Miller et al. 1985); and reacts directly with receptors in the nervous system, such as the acetylcholine receptor in

peripheral nerves. Methylmercury may also arrest the division of neurons during brain development (Sager et al. 1982) perhaps through inhibition of the microtubular system by binding to free sulfhydryl groups on the surface and ends of microtubules (Vogel et al. 1985).

For non-fish consumers, the major source of mercury exposure in the general U.S. population is elemental mercury derived from mercury amalgams. The amount of elemental mercury exposure from dental amalgams is small, and current scientific evidence does not show that exposure to elemental mercury from amalgam restorations poses a health risk in humans, except for an exceedingly small number of allergic reactions (CDC 2001a).

Thimerosal is an ethylmercury containing preservative used in vaccines. Some hypothesized that infants receiving multiple vaccines on a single day could be exposed to a dose of ethylmercury equal to or above USEPA's RfD for methylmercury. However, Pichichero et al. (2002) determined that ethylmercury is eliminated from the blood of infants rapidly with a half-life of 7 days, and the concentration of mercury does not exceed safe levels in infants. Some also proposed a link between autism and exposure to thimerosal contained in childhood vaccines. However, there is no scientific evidence that links exposure to mercury in thimerosal to autism (Nelson and Bauman 2003; Hviid et al. 2003; Stehr-Green 2003; Madsen et al. 2003; Davidson et al. 2004).

Epidemiologic Studies of Chronic Low Level Methylmercury Exposure

Two large-scale epidemiologic studies were designed to help quantify whether subtle neurodevelopmental effects are associated with chronic low-level *in utero* exposures. One study took place in the Seychelles Islands off the coast of Africa and the other in the Faroe Islands in the North Atlantic between Scotland and Iceland. Because of the large sample sizes and the homogeneous nature of both study populations, the studies provide the best opportunity to characterize the magnitude and nature of the risks that may be associated with low-level methylmercury exposure through fish and/or marine mammal consumption. Both studies have been reviewed and critiqued elsewhere (NRC 2001; NIEHS 1998). The results are summarized briefly here.

The Seychelles

In 1989, the University of Rochester, in collaboration with the Seychelles Island Government, initiated a large scale study (the Seychelles Child Development Study) in which the developmental effects of low methylmercury exposure through frequent fish consumption were examined in over 700 women (Cernichiari et al. 1995; Davidson et al. 1995; Davidson et al. 1998; Marsh et al. 1995; Shamlaye et al. 1995). Seventy-five percent of the women indicated eating 10-14 fish meals per week (Shamlaye et al. 1995). Mercury levels in 20 different species of fish (homogenized muscle) ranged from 0.001 ppm for reef fish to 2.04 ppm for Moro shark, and 4.4 ppm for dog tooth tuna (Cernichiari et al. 1995). The overall average fish muscle tissue concentration was 0.3 ppm. Multiple maternal hair samples were collected during pregnancy for quantification of methylmercury exposures. Maternal hair mercury levels were as high as 27 ppm with a median of 6.6 ppm. Maternal hair concentrations did not vary during pregnancy. Maternal hair mercury levels in each trimester correlated with levels representing the entire gestational period, indicating no seasonal differences or peak exposure periods.

Numerous neurodevelopmental tests and physical exams were conducted on the children at 6.5, 19, 29, and 66 months of age. The neurologic evaluation included the Fagan Test, the Revised Denver Development Screening Test, the Bayley Scales of Infant Development, the General Cognitive Index, the Infant Behavior Record, Mental Developmental Index, McCarthy Scales of Children's Abilities, Psychomotor Developmental Index, Preschool Language Scale, and numerous other perceptual, verbal, memory, behavior and motor tests. Physical examinations were also conducted.

No adverse health effects resulting from prenatal or postnatal exposure to methylmercury were noted in the 66-month evaluation (Davidson et al. 1998). In fact, greater prenatal and postnatal exposure to methylmercury enhanced the performance on some test scores, suggesting a beneficial effect of increased fish consumption. A new cohort has been established in the Seychelles to investigate the benefits of fish consumption verses the potential risks of methylmercury exposure (Clarkson and Strain 2003).

In the fifth evaluation (9 years of age) of this cohort, Myers et al. (2003) used "tests previously reported to show (in the Faroe Islands) an adverse association with prenatal exposure to methylmercury." They specifically tested cognition (memory, attention, executive functions) and learning, perceptual, motor, social and behavioral abilities. Of the 21 end-points evaluated, only two showed a significant association with prenatal exposure. One association was adverse (the grooved pegboard, non-dominant hand) and the other association was beneficial (Conner's Teacher Rating Scale, ADHD Index), and both outcomes are probably due to chance. Consistent with the previous evaluations of this cohort, the investigators concluded "the findings do not support an association between prenatal exposure to methylmercury from consumption of large quantities of a wide variety of ocean fish and adverse neurodevelopmental conse-

quences."(Myers et al. 2003; Myers and Davidson 2002). They did find "effects from covariates known to affect child development, but did not find an association with prenatal mercury exposure" (Myers et al. 2003).

Although maternal hair concentrations ranged as high as 27 ppm, all but two women in the study had hair concentrations under 20 ppm, and 659 (80% of the cohort) had maternal hair concentrations less than or equal to 12 ppm. Thus, the Seychelles Islands study is not able to address definitively the extent of risks at the high end of the range of exposures observed in this population.

The Faroe Islands

The other large-scale study took place in the Faroe Islands where methylmercury exposure occurs primarily through consumption of pilot whale meat (1-2 meals a week) containing an average total mercury concentration of 3.3 ppm (1.6 ppm methylmercury) (Grandjean et al. 1994). Of 1,023 consecutive births, the median umbilical cord blood-mercury concentration was 24.2 ppb; 25.1% (n=250) had blood-mercury concentrations that exceeded 40 ppb. The median maternal hair mercury concentration was 4.5 ppm, with 12.7% (n=130) of the women having concentrations exceeding 10 ppm (Grandjean et al. 1992).

Initially, infants (n = 583) were examined for early (0 to 12 months) milestone development (sitting, creeping, and standing). Infants who performed better had significantly higher mercury concentrations in their hair. Better performance and higher hair mercury concentrations were associated with increased frequency of breast-feeding (Grandjean et al. 1995).

Evaluation of the possible *in utero* neurologic effects was made using neurologic and developmental tests conducted at 7 years of age. Tests included the Neurobehavioral Evaluation System (NES) Finger Tapping Test, the NES Hand-Eye Coordination Test, NES Continuous Performance Test, the Tactual Performance Test, the Boston Naming Test for language skills, the Wechsler Intelligence Scale for Children-Revised (WISC-R), WISC-R Digit Spans, WISC-R Block Designs, WISC-R Similarities, Bender Gestalt Test for visuospatial skills, California Verbal Learning Test for memory, and the Nonverbal Analogue Profile of Mood States.

Analyses of 917 children at 7 years of age found no clinical or neurophysiological Hg-related abnormalities. However, subtle decreases in neuropsychological test performance were associated with prenatal Hg exposure at maternal hair levels below 10 ppm, "although test scores obtained by most of the highly exposed children were mainly within the range seen in the rest of the children..." (Grandjean et al. 1997). The long-term predictive value of these findings is not known, and the generalizability of these data to fish consumers is questionable. Interestingly, the Faroese children had excellent visual contrast sensitivity that may be attributed to the ample supply of dietary omega-3 fatty acids.

At age 14 years, Murata et al. (2004) reported an association with prenatal methylmercury exposure and delays in the brain's response to sound, however, hearing thresholds were not affected by methylmercury exposure.

Pilot whales also contain relatively high concentrations of PCBs and organochlorine pesticides. Recently Grandjean et al. (2001) reported neurobehavioral deficits associated with PCBs in this cohort. PCBs were quantified by multiplying the sum concentration of 3 congeners by 2 to derive the total. Four of the neuropsychological outcomes measured showed possible decrements associated with wet-weight PCB concentration, but not lipid-adjusted PCB concentrations. Adjustment for methylmercury reduced the association to a nonsignificant level. The strongest PCB effect was noted in those within the highest tertile of methylmercury exposure. Interestingly, the most sensitive parameter to the PCB exposure was the Boston Naming test; the endpoint selected by USEPA to derive its reference dose (RfD) for methylmercury. USEPA concluded that "…methylmercury neurotoxicity may be a greater hazard than that associated with PCBs, but PCBs could possibly augment the neurobehavioral deficits at increased levels of mercury exposure." Previous statistical analysis by this group indicated methylmercury-associated neurobehavioral deficits were unlikely to be affected by PCB exposure (Budtz-Jorgensen et al. 1999). A consideration of the potential neurobehavioral effects of PCBs and methylmercury suggests further study is needed to conclude the effects noted in the Faroe Islands study are due to methylmercury alone.

The absence of associations in the Seychelles Islands study and the potential confounding affect of PCB exposure on the results of the Faroe Islands study cause continued debate among public health officials as to the appropriate study to use as the basis for dietary guidelines for seafood containing methylmercury.

Potential Cardiovascular Effects from Low-Level Mercury Exposure

Decades of research established the protective effects of fish consumption on cardiovascular disease risk. The American Heart Association recommends consumption of at least 2 fish meals per week (Krauss et al. 2000). The benefits of fish consumption are firmly based upon consistent scientific evidence. Hypotheses of adverse

effects on heart disease from mercury exposure are speculative and unproven.

Recently, scientists hypothesized that low-level methylmercury exposure via the diet may increase the risk of cardiovascular disease. Four recent studies attempted to address this issue, but results are conflicting.

Children

In a Faroe Islands cohort of 1000 seven-year olds prenatally exposed to methylmercury, Sorensen et al. (1999) determined that a rise in cord-blood mercury concentrations of 1 ppb to 10 ppb resulted in an increase in diastolic and systolic blood pressure of 13.9 and 14.6 mm Hg respectively. Above this level no further increase was noted. The significance of this increase is unknown since the average systolic (101 mmHg) and diastolic (64 mmHg) blood pressures noted in those with a blood mercury concentration of 10 ppb and above are similar to worldwide averages (Brotons et al. 1989). Moreover, it is not clear if the change in blood pressure is statistically significant since there were few observations at low cord-blood mercury concentrations. At age 14 years, the effect of prenatal methylmercury exposure on blood pressure was not significant (Grandjean et al. 2004). However, Grandjean et al. (2004) demonstrated that prenatal methylmercury exposure negatively affected cardiac autonomic activity.

Adults

Salonen et al. (1995) studied a cohort of 1,833 Eastern Finnish men over a seven-year period. Historically this cohort experiences an unusually high incidence of mortality from coronary heart disease, even though they consume large quantities of fish. Men in the highest tertile of hair Hg (greater than 2 ppm) had a 2-fold higher risk of acute myocardial infarction compared to men in the lower two tertiles. In earlier studies, these researchers found a relation between selenium deficiency in Eastern Finish men and excess risk of acute myocardial infarction and death from coronary heart disease and cardiovascular disease (Salonen 1982). In general, Eastern Finish men also have a high intake of meat, saturated animal fat, and low intake of vitamin C and other vegetable-derived antioxidants (Salonen et al. 1995).

Guallar et al. (2002) conducted a case control study of 684 men with a first diagnosis of myocardial infarction and 724 controls from eight European countries and Israel. Toenail mercury concentrations were directly associated with the risk of myocardial infarction. Patients in the highest quintile of mercury concentration (0.66 ppm) had an odds ratio of 2.16 (95 percent confidence interval, 1.09-4.29) compared to the lowest quintile (0.11 ppm).

Yoshizawa et al. (2002) did not find a correlation between mercury toenail concentration and the risk of coronary heart disease among 470 male health professionals with documented coronary heart disease and 464 controls. When the highest quintile of mercury concentration (1.34 ppm) was compared to the lowest quintile (0.15 ppm) the relative risk was 0.97 (95 percent confidence interval, 0.63 to 1.50).

Risk Assessment Food Consumption Guidelines

Currently, public health scientists and regulators have not reached a consensus on methylmercury dietary exposure guidelines. For example, the FDA, the Agency for Toxic Substances and Disease Registry (ATSDR), and the USEPA each use different epidemiological studies to derive distinct guidelines (Table 5). The FDA bases their dietary intake guidelines for methylmercury from knowledge gained from the acute poisoning episodes in Minamata and Niigata, Japan and Iraq; ATSDR and USEPA base their dietary guidelines on the Seychelles and Faroe Islands cohorts, respectively. The WHO considers both the Seychelles and Faroe Islands cohorts. Figure 16 summarizes hair mercury guidelines from these agencies.

World Health Organization (WHO)

The WHO recently established a new Provisional Tolerable Weekly Intake (PTWI) for methylmercury of 1.5 µg/kg/week [or a Provisional Tolerable Daily Intake (PTDI) of 0.22 µg/kg/day] based on the results of the Faroe Islands and Seychelles Islands cohort studies (JECFA 2003). The WHO determined a "no observed effect level" (NOEL) relating to subtle neurobehavioral effects from *in utero* methylmercury exposure. The WHO calculated the NOEL of 14 ppm for methylmercury in maternal hair based on the 'critical endpoint' of 12 ppm calculated for the Faroe Islands study and 15.3 ppm calculated for Seychelles Islands study. As noted previously, no effects were attributed to methylmercury exposure in the Seychelles study, and the value of 15.3 ppm represents the mean maternal hair level of mothers in the highest exposure group. Using the standard steady state one-compartment model for methylmercury, and applying an uncertainty factor of 6.4, the NOEL represented by a methylmercury concentration of 14 ppm in hair was converted to the PTDI of 0.22 µg/kg/day. The PTDI corresponds to a hair value of 2.2 ppm and a blood value of 8.7 ppb (JECFA 2003). This PTDI applies to children and women of childbearing age.

The PTDI of 0.5µg/kg body weight per day the WHO reaffirmed for the general populations in 1999 (JECFA

2000) still applies for all other adults. The PTDI was established for adults from the Japanese data, and is based on a lowest observed adverse effect level (LOAEL) for methylmercury in whole blood of 220 ppb (52 ppm hair). WHO used an uncertainty factor of 10 to derive the PTDI. Similarly, the LOAEL of the Iraqi data was 240 ppb to 480 ppb in whole blood. For adults the lowest detectable clinical adverse effect of methylmercury is paresthesia (a numbness and tingling sensation) of the mouth, lips, fingers, and toes. It should be mentioned that the Japanese data were analyzed by the dithizone procedure; however, a later reanalysis of the hair from the patient with paresthesia with the lowest hair mercury concentration (52 ppm), using the newer atomic absorption technique, yielded a value of 82.6 ppm (WHO 1990). All other affected individuals had hair levels above 100 ppm.

Based on available models, a consistent intake of the WHO PTDI (0.5 μg/kg/day) would correspond to a blood concentration of 20 ppb and hair mercury concentrations of 5 ppm. These exposure levels are one tenth of the LOAEL of 220 ppb (blood) depicted in Figure 17.

The 1999 WHO Committee also noted "that fish (the major source of methylmercury in the diet) contribute importantly to nutrition, especially in certain regional and ethnic diets, and recommended that, when limits on the methylmercury concentration in fish or on fish consumption are under consideration, the nutritional benefits are weighed against the possibility of harm (JECFA 2000)."

Food and Drug Administration (FDA)

The FDA followed the approach taken by WHO and derived its action level for commercial sale of 1 ppm in the edible portion of fish based on the Japanese data (Friberg et al. 1971). The FDA calculated the action level for edible portions of seafood for interstate commerce by assuming an acceptable methylmercury daily intake of 0.5 μg/kg body weight per day, a half pound (226 g) of fish consumed per week, and a 70-kg adult, resulting in a tolerance level of 1 ppm (1 ppm =[0.5 μg/kg x 7 days x 70 kg]/226 g of seafood consumption).

Agency for Toxic Substances and Disease Registry (ATSDR)

The ATSDR derived an oral minimal risk level (MRL) of 0.3 μg/kg/day based on the 66-month evaluation of the Seychelles Child Development Study (Davidson et al. 1998). The results of the neurobehavioral and the developmental tests revealed no evidence of adverse effects. Four of six measures showed better scores in the highest methylmercury-exposed groups. The positive outcomes were not considered to indicate any beneficial effect of methylmercury, instead it indicated increased fish consumption (increased methylmercury concentrations correlated with increased fish consumption) and reflected the beneficial effects of omega-3 fatty acids, etc. associated with fish consumption. The mean maternal hair level was 6.8 ppm of mercury. ATSDR arbitrarily selected the mean maternal hair level of 15.3 ppm in the group with the highest exposure to represent the NOAEL and derivation of the chronic oral MRL for methylmercury. An uncertainty factor of 4.5 was used to account for human pharmacokinetic and pharmacodymanic variablity (3.0) and a modifying factor of 1.5 to account for the lack of domain-specific tests used in the Seychelles Islands cohort compared to the Faroe Islands cohort.

ATSDR stated that the modifying factor of 1.5 could be removed if the results of the domain- specific tests in the 96-month Seychelles evaluation are consistent with previous results (i.e., no effects due to methylmercury exposure). As noted earlier, preliminary results of the 107-month evaluation do not support an association between prenatal exposure to methylmercury from uncontaminated ocean fish consumption and adverse neurodevelopmental consequences. Thus, it is reasonable to conclude ATSDR should raise its MRL from 0.3 μg/kg/day to 0.4 μg/kg/day. However, ATSDR is not planning on updating the MRL (Dr. John Risher, ATSDR, personal communication, December 31, 2003).

ATSDR selected the Seychelles Islands study over the Faroe Islands study primarily because the Seychellois diet more closely resembles that of the United States. The Seychellois primary exposure to methylmercury is fish containing concentrations of methylmercury similar to the typical range in the United States (0.004 ppm to 0.75 ppm). The Seychellois, however, consume approximately 10 to 20 times more fish than the U.S. population. In addition, the majority of methylmercury exposure in the Faroe Islands cohort was from pilot whale, with a small portion from fish. Pilot whale contains high concentrations of PCBs and organochlorine pesticides. It is still not clear to what degree concurrent *in utero* exposure to PCBs influenced the outcome of the neurobehavioral tests in the Faroe Islands study (ATSDR 1999, NRC 2000, Grandjean et al. 2001). The Seychelles Islands cohort did not have a significant exposure to PCBs.

United States Environmental Protection Agency (USEPA)

The USEPA (2001) calculated its reference dose (RfD) of 0.1 μg/kg/day for methylmercury using the results of the Faroe Islands study (Grandjean et al. 1997 and 1998). Grandjean et al. (1997) reported "significant associations between either maternal hair mercury or cord-blood

mercury and decrements in several neuropsychological measures." The USEPA selected the Boston Naming Test as the critical endpoint. To estimate the level of exposure or dose that is associated with an increase in adverse effects; the USEPA relied on the statistical analysis performed by Butdz-Jorgensen et al. (1999). They calculated a benchmark dose concentration (BMD) of 85 ppb. The BMD is the lowest dose estimated from the statistically modeled data that is expected to be associated with a small increase (in this case 5%) in the incidence of adverse outcome. To derive their RfD, USEPA used the lower 95% confidence limit (termed the BMDL) on the BMD (85 ppb), which was 58 ppb (USEPA 2001). Using current models and applying an uncertainty factor of 10, USEPA converted the BMDL (58 ppb) to a RfD of 0.1 μg/kg/day. This is identical to the RfD USEPA derived from Iraqi data (Marsh et al. 1987). The RfD of 0.1 μg/kg/day corresponds to a hair concentration of 1.2 ppm and a blood concentration of 5.8 ppb.

Health Canada

Health Canada has derived a provisional tolerable daily intake (PTDI) for women of reproductive age and infants of 0.2 μg/kg body weight/day, and they use 0.5 μg/kg/day for other adults (NRC 2000). Based on the recent epidemiological data, Health Canada established a provisional no observed adverse effect level of 10 ppm Hg in maternal hair. By applying an uncertainty factor of 5 to account for interindividual variability; Health Canada derived the PTDI of 0.2 μg/kg/day (NRC 2000). For biomonitoring studies, Health Canada applies the following ranges: a blood mercury value of ≤ 20 ppb is normal, 20 ppb to 100 ppb is the level of concern, and greater than 100 ppb is their action level (Van Oostdam et al. 2003; AMAP 2003). A blood value of 20 ppb corresponds to 5 ppm in hair.

Arctic Monitoring and Assessment Programme

Since 1991, the international Arctic Monitoring and Assessment Programme (AMAP) has been evaluating the potential human health impacts of exposures to arctic contaminants such as mercury and PCBs (AMAP 2002; 2003). Public health officials from AMAP and other arctic scientists concluded that the nutritional and physiological health benefits of traditional arctic subsistence foods outweigh potential risks in most areas of the Arctic, and advise local public health policy makers to encourage continued traditional food use when indicated by risk-benefit analyses (AMAP 2002; 2003).

This was recently highlighted at the 2002 AMAP meeting in Rovenemi, Finland by Jay Van Oostdam of the AMAP human health working group, and at the 2002 Arctic Council meeting in Saariselka Finland by Helgi Jensson, AMAP Chair. They also stated that methylmercury intake guidelines should be used by public health officials only as tools to craft dietary advice, not as a strict standard. The AMAP pointed out the USEPA reference dose for methylmercury only considers the potential risks and does not take into account the well-known benefits of fish consumption.

This concept was applied recently in Nunavik (Arctic Quebec). Dewailly et al. (2001a) determined the exposure of Nunavik residents to methylmercury. Overall, women had a geometric mean methylmercury blood concentration of 16.6 ppb (range 2 ppb to 112 ppb). The concentration increased with age. Although a number of individuals potentially exceeded the Canadian blood methylmercury benchmark of 20 ppb, local health officials did not restrict seafood consumption because their diet is also rich in selenium (e.g., beluga whale skin), that is suggested to protect against methylmercury induced toxicity (Dewailly et al. 2001a).

Dietary Intake of Methylmercury in Alaska

Exposure Estimates

The primary route of human exposure to methylmercury in Alaska is ingestion of fish and marine mammals. At this time, it is difficult to estimate the current exposure of Alaskans to methylmercury because little dietary intake data are available, although there are a number of dietary surveys underway.

For Inuit from Greenland and Canada available methylmercury or total mercury monitoring data of subsistence species plus dietary intake data among subsistence users indicate that the current WHO's provisional tolerable weekly intake of 90 μg for methylmercury may be occasionally exceeded by a significant proportion of those populations (Johansen et al. 2000; AMAP 2003).

Similarly, for Alaska it is very likely that a portion of the population eats fish and shellfish several times a week, particularly during fishing season. In a dietary survey of Alaska Natives, fish ranked high in the list of frequently eaten foods (Nobmann et al. 1992). Among all seafood, salmon ranked highest in the species most often consumed. The mean of the daily intake of fish and shellfish for Alaska Natives was 109 g (i.e., 3.82 ounces) compared with a mean daily intake of 32 g used by FDA to derive its tolerance level for commercial seafood products of 1 ppm.

The Community Profile Database (ADFG 2001) maintained by the Division of Subsistence Alaska Department of Fish and Game, presents harvest rate information for a number of villages throughout Alaska. Figure 18 depicts the regional harvest of subsistence

resources in Alaska. Harvests rates can provide a rough estimate of the relative amount of resources consumed. However, consumption rates may be higher or lower than reported harvest rates based on a number of factors (ADFG 1996). Table 6 and 7 present harvest data (per capita pounds) and percentage of total edible weight (of all resources harvested) for the top 5 resources in the 5 subsistence regions of Alaska for fish and marine mammals, respectively. By comparing the top fish resources harvested in Table 6 (salmon, whitefish, herring, halibut, Dolly Varden, and sheefish) to the methylmercury concentration data in Figures 2-15 it is clear that subsistence users are mainly harvesting fish that contain relatively low levels of methylmercury.

For marine mammals, the main harvested species include bearded seal, bowhead whale, walrus, harbor seal, fur seal, ringed seal, and beluga. Except for beluga tissues and liver and kidney tissues of some marine mammals, the total mercury concentrations in these marine mammals are below the FDA action level of 1 ppm (Table 3 and 4). For liver and kidney tissues, methylmercury contributes only 2% to 12% of the total mercury concentration. Only the beluga and fur seal liver or kidney approach or exceed 1 ppm methylmercury.

Table 8 presents commercial harvest data recorded by the Alaska Department of Fish and Game, Division of Commercial Fisheries (personal communication with Michael Plotnick ADFG, 2002). A comparison of the top species harvested to the methylmercury concentrations in Figure 2 to Figure 15 and Table 2 indicates these species contain relatively low concentrations of methylmercury. Overall, the above data indicate that methylmercury concentrations in fish harvested from Alaska waters are relatively low.

ADPH calculated the allowable amount of different seafood products that could be consumed for an average weight 67-kg woman of reproductive age based upon USEPA's methylmercury RfD, and the WHO's methylmercury PTDI (Table 9). The amount that could be consumed based on the EPA and WHO 'critical endpoints' used to calculate the RfD and the PTDI is also presented (i.e., the BMDL and the NOEL not including the uncertainty factors of 10 and 6.4). In addition, consumption based on the WHO PTDI for other adults is presented. Alaskan fish and marine mammal methylmercury tissue concentrations were utilized for the calculation of average allowable consumption.

Fish and marine mammals are nutritious food items and negative changes in health status have been observed in populations where food consumption advisories have been applied resulting in social and economic changes (Shkilnyk 1985). Therefore, the need for and implications of issuing food consumption advisories based upon the WHO PTWI or the USEPA RfD must be carefully examined in context of the magnitude and implications of the benefits of consuming these foods and in context of the magnitude of error in extrapolating risks of exposures to contaminants in these foods (Egeland and Middaugh 1997).

Factors that May Modify Possible Methylmercury Toxicity

Methylmercury exposures through the arctic food chain represent chronic low-level exposures. Dietary factors associated with methylmercury in fish and marine mammals may play an important role in toxicity and absorption of methylmercury. For example, mice fed methylmercury chloride with cod liver oil absorbed significantly less methylmercury than a comparison group of mice fed coconut oil or soy oil (Hojbjerg et al. 1997). Also, high amounts of soy and fish protein reduced methylmercury absorption compared to low protein diets in the laboratory mice (Hojbjerg et al. 1997).

Also, a number of dietary factors may modify the toxicity of methylmercury. Vitamin E, for example, may be an important dietary component that modifies methylmercury toxicity. Vitamin E is a well-known antioxidant and may provide protection against toxic effects of methylmercury on biological membranes through the prevention of membrane degradation (Chang et al. 1978). In studies of quails and rats, vitamin E improved growth rates and increased life span compared to animals exposed to methylmercury alone (Welsh et al. 1976). Also, vitamin E protected nervous tissue (*in vitro*) from the toxic effects of methylmercury (Kasuya 1975). In another study, hamsters fed vitamin E with methylmercury chloride showed none of the morphological signs of toxicity on nervous system tissues (such as neuronal necrosis in the cerebellum and calcarine cortex) that were observed in hamsters fed methylmercury chloride alone (Chang et al. 1978).

Fish is a good source of vitamin E compared to other sources of animal protein. Salmon steak contains 1.8 mg/100g of vitamin E (measured as total tocopherols), shrimp (frozen, baked) contains 6.6 mg/100g, scallops (frozen, baked) contain 6.2 mg/100g, and haddock filet (broiled) contains 1.2 mg/100g of vitamin E (Bauernfeind 1980). In contrast, other dietary sources of protein contain lower levels of vitamin E: bacon (0.59 mg/100 g), bologna (0.49 mg/100 g); salami (0.68 mg/100 g); and chicken (0.58 to 1.39 mg/100 g) (Bauernfeind 1980).

Vitamin C may also be an important component of the diet that may modify methylmercury toxicity. Guinea pigs on a vitamin C deficient diet suffered more neurological damage when exposed to methylmercury

than a comparison group of guinea pigs fed a diet with adequate vitamin C (Yamini et al. 1984). Thus, numerous dietary factors may alter methylmercury toxicity.

Selenium and Methylmercury Exposure

Levels of selenium within the range of nutritional requirements for dietary selenium may be highly effective in reducing the toxicity of methylmercury (Ganther et al. 1972). But while the literature is promising, it is not conclusive and human data are lacking. Chapman and Chan (2000) recently reviewed animal studies from the last two decades. One of the most notable early experiments found that Japanese quail given methylmercury in diets containing 17% tuna survived considerably longer than quail given the same amount of methylmercury (which was lethal) in a corn-soya diet (Ganther et al. 1972). The selenium content of tuna was thought to protect the quail from methylmercury toxicity. Since that study, many reports have become available describing the antagonism between selenium and mercury (Chapman and Chan 2000). For example, in a rat feeding study, all rats given mercury in their drinking water without a selenium supplement died at the end of a 6-week period, while those fed mercury with selenium survived. In another study, sodium selenite protected offspring of mice from the neuro-developmental effects on reflexes that had been observed in the offspring of mice exposed to methylmercury alone (Satoh et al. 1985).

In a recent study with human subjects, Seppanen et al. (2000) examined the effect of organic selenium supplementation on mercury status of individuals with low serum selenium (Se < 90 ppb). Individuals (n=13) given 100 μg of a yeast-based selenium supplement for four months had a statistically significant decrease in pubic hair mercury concentrations compared to controls (n=10). Pubic hair mercury levels decreased from 0.42±0.16 ppm to 0.27±0.17 ppm. This study indicates a potential interaction between selenium and methyl-mercury in humans. But, this study was not designed to determine if selenium supplementation yielded a protective effect against methylmercury toxicity.

As mentioned previously, Dewailly et al. (2001a) reported that local health officials in Nunavik (Arctic Quebec) did not restrict seafood consumption in the population that had a blood methylmercury concentration ranging from 2 ppb to 112 ppb because its diet was rich in selenium (e.g., beluga whale skin).

The mechanisms by which selenium protects organisms from methylmercury toxicity are not fully understood. Substantial evidence suggests that selenium actually enhances whole body retention and accumulation of methylmercury in the brain (Stillings et al. 1974; Chen et al. 1975; Ohi et al. 1975; Magos et al. 1977; Alexander et al. 1979; Magos et al. 1987; Hansen 1988). It should be noted, however, that the form of selenium appears to influence the organ distribution and speciation of mercury in animal studies. For instance, in one study, the administration of inorganic selenite with Hg resulted in a greater proportion of total mercury in tissues than after a dose of organic selenium (Magos et al. 1984). Various mechanisms may also play a role in the protective effect of selenium against metal toxicity. Some hypothesize that selenium's protective effect is attributed to selenium and mercury forming a biologically inactive compound (Groth et al. 1976; Naganuma et al. 1981; Magos et al. 1987; Hansen 1988). However, since small amounts of selenium are protective against larger amounts of mercury, others suggest that the magnitude of protection is probably explained by other mechanisms (Ohi et al. 1980), such as the ability of selenium to protect neuronal tissues against methylmercury toxicity through its role in the antioxidative process (Chang et al. 1982). Evidence for this mechanism comes from the finding that rats fed methylmercury for six weeks showed a marked suppression in glutathione peroxidase (GSH-Px) activity, while rats exposed to both methylmercury and selenium showed no significant alteration in GSH-Px activity (Chang et al. 1982).

Further work is needed to characterize better the extent to which selenium is protective of methylmercury toxicity at dosages commonly found in fresh and saltwater fish. Selenium at high doses is toxic and some discrepancies in the protective effect of selenium-mercury feeding studies may be, in part, attributed to the relatively high levels of selenium and mercury used in the animal studies. Also, the half-life of selenium is considerably shorter than that of methylmercury and may help explain why selenium's protective effect disappears over time in some high dose methylmercury feeding studies.

Selenium Concentrations in the Environment

The concentration of selenium in unpolluted ocean waters is under 1 ppb (Ihnat et al. 1989). Selenium in the earth's crust is not uniformly distributed, however, and some geographical areas have deficient amounts of selenium in the soil and plant life (ATSDR 1999). Marine fish and mammals accumulate selenium through the food chain, while crustaceans absorb selenium directly from water and sediments (Ihnat et al. 1989). In general, selenium concentrations in marine fish, shellfish, and marine mammals are higher than those found in terrestrial animals or fresh water fish (Ihnat et al. 1989). Most marine fish species contain average selenium concentrations ranging from 0.4 to 0.9 ppm (Hall et al. 1978). The concentration of selenium in muscle of king

and chum salmon collected from the Yukon and Kuskokwim Rivers ranged from 0.06 to 0.37 ppm (USFW 2003). The liver and kidney tissues of marine fish and mammals and the hepatopancreas of shellfish usually contain the greatest concentrations of selenium (Guinn et al. 1974; Grieg et al. 1976; Chou et al. 1978; Shultz et al. 1979; Luten et al. 1980; Wrench et al. 1981).

In marine mammals and in some studies of marine fish, a number of researchers have found that mercury and selenium accumulate in livers and kidneys in a one-to-one molar ratio (Ganther et al. 1972; Koeman et al. 1975; MacKay et al. 1975; Kari et al. 1978; Shultz et al. 1979; Tamari et al. 1979; Ganther 1980; Wagemann et al. 1998; Deitz et al. 2000). It had been hypothesized that the formation of mercury:selenium complexes is a probable mode of mercury detoxification in marine mammals (Wagemann et al. 1998). As mentioned previously, marine mammals have the ability to demethylate methylmercury to inorganic mercury (Hg^{2+}). The one-to-one molar ratio is a result of a relatively quick demethylation step (methylmercury half-life is 20 to 500 days in ringed seal liver) and subsequent complexation with selenium, which accumulates with age (Wagemann et al. 1998).

However, recent studies in Alaskan bowhead whales, beluga whales, ringed seals and polar bears have not corroborated the one-to-one molar ratio. The molar ratio of mercury:selenium was less than one for all species (Woshner et al. 2001a; 2001b). Woshner et al. (2001a; 2001b) indicated their results did not counter the recognized relationship between mercury and selenium, but they hypothesized that a molar ratio of one-to-one may only be present when a physiologic threshold has been surpassed or that adherence to this ratio is not necessary for protection against mercury toxicity. They present an excellent summary of those studies supporting and refuting the one-to-one molar ratio in marine mammals.

In contrast to selenium in marine mammals, selenium concentrations in most marine fish are usually several times higher than those of mercury (Freeman et al. 1978; Cappon et al. 1981; Cappon et al. 1982; Ihnat et al. 1989). The molar ratio of selenium to mercury in king and chum salmon collected from the Yukon and Kuskokwim Rivers ranged from 3:1 to 25:1 (USFW 2003). Fish exposed to mercury-polluted waters, however, contain considerably more mercury than selenium (a 10:1 ratio), indicating that in areas of environmental pollution the uptake of mercury exceeds that of selenium (Beijer et al. 1978). Table 10 depicts the selenium tissue concentrations summarized from the published literature in Alaskan marine mammals.

Inorganic vs. Organic Mercury in Liver and Kidney Tissues

The liver and kidney of marine mammals can contain relatively high levels of mercury, the majority of which is inorganic. While it may be possible for inorganic mercury to be methylated by intestinal bacteria in humans (Rowland et al. 1975), this is not thought to happen to a large extent because inorganic mercury does not readily cross cell membranes and is readily excreted. In a laboratory study, cats fed ringed seal liver showed no neurologic or histopathologic abnormalities associated with mercury exposure, while cats fed beef liver plus methylmercury chloride developed the neurologic and histologic signs of mercury toxicosis within 90 days (Eaton et al. 1980). The total mercury intake from the seal liver was quite high (up to 158 mg over 90 days), while the total mercury intake from the beef liver with methylmercury chloride exposure group was lower (80 to 90 mg). Only a small percentage of the total mercury in the seal liver was organic, 3%. Tissue accumulation of mercury in the tissues of the cats reflected the organic fraction and not the high inorganic fraction of total mercury in the seal liver. Selenium levels in the liver and kidney of the cats fed ringed seal liver indicated that selenium levels increased with increasing levels of methylmercury. Such an increase was not observed in the cats fed beef livers with methylmercury chloride.

Methylmercury Levels in Alaskans

Many factors influence the accuracy of risk assessments based upon fish tissue concentrations of mercury. Biomonitoring using hair or whole blood mercury concentrations can better quantify the levels of mercury exposures in a population (NRC 2000; Myers et al. 2003; JECFA 2003; Harkins and Sustin 2003; CDC 2001b). To that end, several human exposure studies have been conducted in Alaska since the 1970s (Table 11). Overall, results indicate that average concentrations are below the WHO No Observed Effect Level (NOEL) for women of childbearing age of 14 ppm in hair and 56 ppb in blood.

The Centers for Disease Control and Prevention (CDC) conducted a study of mercury exposure among residents of the Pribilof Islands in 1970 (Hochberg et al. 1972). Mean hair total mercury content was similar among Alaska Natives eating fur seal liver at least once a week in 1970 (5.6 ppm, n=15), Natives who did not eat liver (4.9 ppm, n=13) and Caucasians who did not eat liver (3.4 ppm, n=6). The presumed high inorganic mercury content of mercury in liver (relative to methylmercury) may account for the lack of a significant difference in hair mercury concentration between consumers and non-consumers of fur seal liver. The highest hair mercury level (16.2 ppm) was found in a resident of the Pribilof Islands in 1970.

In 1972, DPH conducted an investigation of 145 Alaskans to determine whether exposure to mercury through the diet posed a potential health hazard (ADPH 1972). Total mercury was determined in red blood cells, plasma and hair. Of the 91 hair mercury measurements, the mean mercury concentration in the hair of Pribilof Island residents (n = 13) was 5.8 ppm, while the average hair mercury concentration of new mothers in Bethel was 5.1 ppm (n = 14). These concentrations were higher than those found in Juneau (1.5 ppm, n = 8) and in villages along the Yukon and Kuskokwim Rivers (1.2 ppm, n = 56). No overt signs of toxicity to the study population were observed.

A study of maternal-infant pairs for mercury exposure was conducted in the mid-1970s (Galster 1976). Hair, milk and blood from 38 mother-infant pairs from the Yukon-Kuskokwim coast and interior, and from Anchorage were analyzed for mercury concentrations. Of the 22 maternal hair measurements made, results demonstrated no difference in hair mercury content between the coastal (4.3 ppm, n=12), interior (3.6 ppm, n=6) and urban (4.0 ppm, n=4) areas. Maternal and child plasma mercury levels did show a trend, however, with the highest mercury content in the coastal group, and the lowest content in the Anchorage group. For example, mean maternal mercury levels measured in red blood cells were significantly higher in the coastal area (33.5 ppb, n=17), when compared to the interior (22.6 ppb, n=11), and urban (8.9 ppb, n=10) areas. Other parameters, such as infant birth weight and Apgar scores were not significantly different by geographic area.

A study of 200 samples from women of childbearing age collected in Nome from September to October 1989 evaluated total hair mercury (Crecelius et al. 1990). This study found low mercury content in the hair (average = 1 ppm, range 0.02 ppm to 8.0 ppm). Only 12 samples were above 3.0 ppm mercury in hair. A follow-up study conducted segmental analysis of hair from 80 Nome women obtained in the fall of 1990 (Lasorsa et al. 1991). This study also found low mercury levels (average concentration = 1.4 ppm) in the hair of the Nome women. Unfortunately, no attempt was made to characterize dietary intake of fish and marine mammals in the women participating in the study. However, it was reported that 53 of the 80 participants were heavy subsistence food consumers (Lasorsa et al. 1991).

Rothschild and Duffy (2002a) determined the concentration of methylmercury in the hair of 16 (11 female and 5 male with a mean age of 49) rural Alaskan subsistence food users from Napakiak, located on the Kuskokwim River in southwest Alaska. The results were compared to 20 (16 female and 4 male with a mean age of 31) adult non-subsistence food users from Fairbanks. The mean methylmercury hair concentration for Napakiak was 1.5 ppm (range of 0.32 ppm to 4.0 ppm). The Fairbanks population had a mean concentration of 0.19 ppm (range of 0.03 ppm to 0.43 ppm). No attempt was made to determine specific dietary history of any individual in the study. By comparing the results to Galster's study in the mid-1970s, the authors concluded, based on the limited sample size, that mercury concentrations have not increased over the last 25 years.

As a follow-up, Rothschild and Duffy (2002b) sampled subsistence foods from Napakiak for methylmercury. Concentrations ranged from 0.001 ppm to 0.44 ppm, with dried pike having the highest concentration. This limited subsistence food sampling indicates methylmercury concentrations are not high enough to pose a health risk as reflected in the hair monitoring data.

The Alaska Native Tribal Health Consortium (ANTHC) is conducting an infant-maternal cord blood study in partnership with several regional health corporations. To date, 81 samples have been collected at the time of delivery from mothers from the Barrow and Bethel areas (Berner 2003). Average total mercury concentrations were 1.5 ppb (range = not detected - 4.5 ppb) for Barrow (n = 29) and 6.5 ppb (range = 0.6 ppb – 21 ppb) for Bethel (n = 52) (Table 12). These average concentrations are well below the Health Canada guideline of 20 ppb and the WHO NOEL of 56 ppb. The small difference in mercury levels from the two areas probably reflects distinct diets. Mothers from the Barrow area consume terrestrial mammals and bowhead whales that have lower levels of methylmercury, whereas mothers from the Bethel region potentially consume fresh water predatory fish such as pike and burbot and marine mammals such as seals and beluga. ADPH (2002a) analyzed hair samples from 6 individuals from Yukon-Kuskokwim Delta villages and 3 individuals from North Slope villages that participated in the ANTHC study (Table 11). Consistent with previous results for rural Alaskans, hair mercury concentrations were very low. Arithmetic mean hair total mercury concentrations were 0.91 ppm with a range of 0.29 ppm to 1.9 ppm; well below the WHO NOEL of 14 ppm.

The Alaska Division of Public Health's response to the concerns of food safety among Alaskans has been to implement the Statewide Maternal Hair Mercury Biomonitoring Program to estimate exposure levels of methylmercury. The program offers free and confidential hair mercury testing to all pregnant women in Alaska (ADPH 2002b). The program also supports targeted testing of all women of childbearing age in areas of the state where relatively more fish and/or marine mammals are consumed. As of October 1, 2004, the ADPH received 237 hair samples from 39 Alaskan communities (Figure 19). Since participation in the program is

voluntary, our preliminary results are not representative of the Alaska population. The median and mean hair mercury concentrations for pregnant women (n = 176) were 0.47 ppm and 0.71 ppm (range 0.02 – 6.35 ppm) (Figure 20). The median and mean hair mercury concentrations for WCBA (n = 60) were 0.63 ppm and 1.2 ppm (range 0.15 – 8.36 ppm). The value of 180 ppm was excluded from the statistical analysis, because this woman was not from Alaska, she reported she did not consume Alaska fish, and additional investigation determined that external contamination was the cause of her high value. She showed no symptoms of mercury toxicity and her blood level was 23 ppb.

Hair and blood mercury concentrations observed in Alaskans have been lower than anticipated based upon the frequency of fish and marine mammal consumption and subsistence food mercury concentrations. Reasons for this discrepancy are unknown. However, the laboratory mice studies in Denmark showing reduced absorption of methylmercury when co-administered with cod liver oil or high protein diets suggest that our understanding of methylmercury is still emerging (Hojbjerg et al. 1997). The Alaska Native diet is both high in fish and marine oils and animal protein. Another possible explanation is that Alaskans mainly consume fish and marine mammal tissues containing low concentrations of methylmercury. Recently initiated dietary surveys should shed some light on actual consumption patterns.

Compared to other areas in the Arctic, levels of methylmercury in Native Alaskans are lower than indigenous populations of Greenland and Baffin and Nunavik in Eastern Canada (Table 12), where local public health officials have continued to endorse the unlimited use of traditional foods (AMAP 2002). The President of the Inuit Circumpolar Conference in Canada, Mr. Duane Smith, confirmed this at the 2002 Arctic Council Meeting in Saariselka, Finland (Reuters, October 11, 2002).

People living in the lower 48 states have lower exposure to methylmercury most likely because they consume less fish. CDC recently published the 1999 National Health and Nutrition Examination Survey (NHANES) results for hair (CDC 2001) and blood mercury (Schober et al. 2003) concentrations for children age 1 to 5 years and women of childbearing age 16 to 49 years. These data constitute a representative population sample for the United States but are not representative of U.S. subpopulations with high fish ingestion. The geometric mean blood-mercury concentrations for children (n = 705) and women (n = 1709) were 0.34 ppb and 1.0 ppb, respectively. The 95th percentile concentration was 2.3 ppb and 7.1 ppb, respectively. Inorganic mercury was not detected in the blood samples; therefore, these concentrations represent methylmercury. The geometric mean total mercury concentrations for hair samples of children age 1 to 5 years (n = 338) and women of childbearing age 16 to 49 years (n = 702) were less than the limit of detection (0.1 ppm) and 0.2 ppm, respectively. The 90th percentile total mercury concentrations were 0.4 ppm and 1.4 ppm, respectively.

Overall, the available data suggest that exposure levels to methylmercury in Alaska, are below the WHO NOEL of 14 ppm in hair or 56 ppb in blood. Screening programs underway will better characterize exposures in all geographic areas of Alaska. Communities consuming large quantities of piscivorous fish such as pike or carnivorous marine mammals such as sea lions or belugas should be the focus of future screening efforts.

Alaska's Perspective on USEPA and FDA National Fish Advisories

The national generic fish consumption advisories recommending women of childbearing age to restrict consumption of recreationally caught fish to 6 ounces per week (USEPA) and commercially caught fish to 12 ounces per week (FDA) are not appropriate for Alaska. This "one-size-fits-all approach" is not consistent with available scientific evidence and may result in harming public health.

First, the concentrations of methylmercury detected in the most frequently consumed fish in Alaska (e.g. king, silver, chum, red, and pink salmon) are very low (< 0.05 ppm), and much more than 6 ounces per week can be consumed. Considering even the most conservative USEPA model, one could safely consume 2.1 pounds (33.6 ounces) per week of fish containing 0.05 ppm methylmercury (Table 9). This value (2.1 pounds) assumes a 10-fold uncertainty factor (Table 9).

Second, scientists, medical, and public health professionals do not agree on safe levels of dietary intake of methylmercury to protect the developing fetus (Table 9). USEPA chose to base its recommendations for dietary methylmercury exposure primarily upon the data from the Faroe Islands study where subtle, non-clinical decreases in neurodevelopmental outcomes were noted in mothers who were primarily exposed to methylmercury through the consumption of pilot whale meat (1-2 meals a week; average methylmercury concentration 1.6 ppm), which also contained high levels of PCBs and chlorinated pesticides (Grandjean et al. 1997). Since it is hypothesized that PCBs may cause similar effects, it is difficult to separate the contributions of PCBs and methylmercury in this study population.

The USEPA chose not to consider the results of the Seychelles Islands study where no adverse effects were

established in children of mothers who routinely consumed 10-14 fish (average methylmercury concentration of 0.3 ppm) meals per week and had a median methylmercury hair concentration of 6.6 ppm (equals approximately 26 ppb in blood) (Myers et al. 2003). In the 66-month evaluation of the Seychelles cohort, positive neurodevelopmental outcomes were associated with increased prenatal and postnatal mercury exposure. This effect was not attributed to methylmercury exposure, but to increased fish consumption and the associated beneficial nutrients (Davidson et al. 1995). A new cohort has been established in the Seychelles to investigate the benefits of fish consumption verses the potential risks of methylmercury exposure (Clarkson and Strain 2003).

Third, human biomonitoring results from Alaska including the Alaska Division of Public Health's Statewide Maternal Hair Mercury Biomonitoring Program and the Alaska Native Tribal Health Consortium's infant-maternal cord blood study indicate that methylmercury concentrations in hair and blood of women of childbearing age (WBCA) are well below the WHO NOEL of 14 ppm in hair or 56 ppb in blood (Table 11 and 12, Figure 19 and 20).

Lastly, these national fish advisories are based upon risk assessment without consideration of well-established public health benefits of fish consumption and the potential harm to public health if reductions in fish consumption occur (Egeland and Middaugh 1997). The subsistence lifestyle and diet are of great importance to the self-definition, self-determination, cultural and socio-economic, and overall health and well-being of indigenous peoples. Alaska Natives have voiced their fears and concerns about the safety of traditional foods. However, Native elders have also expressed concerns that the fear associated with the contaminants may cause greater harm than the actual presence of the contaminants themselves and that health warnings regarding food consumption should only be made when there is strong evidence that the risks outweigh the benefits.

Established health benefits of consumption of fish or marine mammals include protection from cardiovascular disease (Albert et al. 2002; Dewailly et al. 2001b; Harris and Isley 2001) and diabetes (Alder et al. 1994), improved maternal nutrition and neonatal and infant brain development (Allen and Harris 2001; Uauy-Dagach and Mena 1995; Uauy et al. 1996), and potential prevention of cancers of the gastrointestinal tract and prostate gland (Terry et al. 2001; Augustsson et al. 2003; Fernandez et al. 1999).

Adverse effects on public health and communities from fish advisories with subsequent abandonment of traditional diets are well documented (Egeland and Middaugh 1997; Kuhnlein et al. 2001; Ebbesson et al. 1999). Currently, Alaska Natives are experiencing a major increase in the prevalence of diabetes (Ebbesson et al. 1999) and overweight/obesity (Wertz-Stein 2003). Recent studies have documented vitamin D deficiencies (Gessner et al. 2003). In addition, Alaskans are faced with serious problems of alcohol use and lack of physical exercise (Rarig et al. 2001). All these conditions are potentially linked to abandonment of a traditional diet and lifestyle.

In response to the national USEPA and FDA fish advisories of January 2001, the ADPH engaged in extensive consultations with Alaska stakeholders. After reviewing all of the available evidence, the ADPH issued consensus recommendations for fish consumption in Alaska (ADPH 2001b). The most important difference from national advisories is that:

> "The Alaska Division of Public Health continues to strongly recommend that all Alaskans, including pregnant women, women who are breast-feeding, women of childbearing age, and young children continue unrestricted consumption of fish from Alaskan waters."

The State of Alaska does not support:

- national advisory recommendations to restrict fish consumption to 12 ounces/week; or
- national advisory recommendations for pregnant women to restrict fish consumption to one meal/month.

The following agencies and organizations endorsed these recommendations:

Alaska Department of Environmental Conservation

Alaska Department of Health and Social Services

Alaska Native Health Board

Alaska Native Science Commission

Alaska Native Tribal Health Consortium

Aleutian/Pribilof Islands Association, Inc.

Institute for Circumpolar Health Studies, University of Alaska, Anchorage

North Slope Borough

University of Alaska, Fairbanks

Yukon Kuskokwim Health Corporation

Summary

- Mercury is a natural element that is ubiquitous in the environment;
- Anthropogenic releases of mercury have increased since the industrial revolution and roughly equal natural releases;
- The most frequently consumed fish from Alaska, such as salmon, cod, halibut, pollock, sole, and herring contain very low concentrations of methylmercury. Methylmercury concentrations in salmon are among the lowest reported;
- Currently, there is good agreement worldwide regarding safe levels of dietary methylmercury intake for adults. Controversy exists, however, regarding the most appropriate guidelines for dietary intake of methylmercury to protect the developing fetus;
- The general national fish advisories issued by USEPA and FDA are inappropriate for Alaska and are not consistent with Alaska recommendations;
- Extensive scientific research has documented the numerous health, social and cultural, and economic benefits of eating fish;
- Eating fish provides inexpensive and readily available nutrients, vitamins, essential fatty acids, antioxidants, calories and protein that contribute to significant health benefits;
- Proven health benefits include protection from cardiovascular disease and diabetes, and improved maternal nutrition and neonatal and infant brain development;
- The subsistence lifestyle and diet are of great importance to the self-determination, cultural, spiritual, social, and overall health and well being of Alaska Natives;
- The preponderance of data indicates the known benefits of fish consumption far outweigh the theoretical and controversial potential adverse health effects from methylmercury found in Alaska fish; and
- Substitution of other less healthy, less nutritious food for Alaska fish would result in far greater harm to health.

The ADPH continues to strongly recommend that all Alaskans, including pregnant women, women who are breast-feeding, women of childbearing age, and young children continue unrestricted consumption of fish and marine mammals from Alaskan waters.

Recommendations

Because many scientific questions about methylmercury and the subsistence diet remain, the Alaska Division of Public Health recommends the following research to help provide the information needed for the ongoing evaluation of the safety of marine mammal and fish consumption in Alaska:

- Increasing human exposure assessments as proposed by the National Center for environmental Health (NCEH) through expanding the National Health and Nutrition Examination Survey assessments to the State level;
- Expanded biomonitoring for methylmercury exposure through whole blood or hair analyses, particularly among women of reproductive age and among high consumers of fish and seafood in different geographic areas of the state;
- Laboratory research exploring the dietary factors such as vitamin E and C, selenium, protein and fish oils on the pharmacokinetics and toxicity of methylmercury;
- Trace metal monitoring of marine mammal species with a greater emphasis on clarifying the ratio of methylmercury to total mercury for each species by tissue type, and additional characterization of organic mercury compounds and their bioavailability and toxicity;
- Fish methylmercury monitoring studies, particularly for inland watersheds; and
- Analysis of prepared subsistence foods to determine concentration changes following cooking and and processing.

Based upon the full range of information available, the ADPH supports unlimited consumption of fish and marine mammals as part of a balanced diet. Fish and marine mammals provide an inexpensive and readily available source of nutrients, essential fatty acids, antioxidants, calories, and protein to Alaska residents and Native peoples and may provide health benefits such as protection against diabetes, cardiovascular disease, and improved maternal nutrition and neonatal and infant brain development. Fish and marine mammals can provide an important component to a healthy varied diet consisting of other sources of protein, such as game meats, grain products, vegetables and fruit.

Table 1. Total mercury and methylmercury (ppm) in ancient human hair from circumpolar regions.

Location	Date (A.D.)	Number of samples	Mean concentration Total mercury	Methylmercury	Reference
Karluk One Kodiak, Alaska	1160-1660	16	1.3	0.03	Egeland et al. 1999
Barrow, Alaska	1460	2	3.0	NA	Toribara and Muhs 1984
N. Baffin Island, Canada	400-1150	8	NA	1.7	Wheatley and Wheatley 1988
Umanak, Greenland	1400	6[a] 2[b]	3.1 10	NA NA	Hansen et al. 1989
Kagamil Island, Aleutian Islands, Alaska	1445	4[a] 5[b]	5.8 not reported[c]	1.2 1.4	Middaugh et al. 2002

NA = not analyzed
[a]adults
[b]children
[c]mean total mercury concentrations were not reported because of extreme external mercury contamination for some samples

Table 2. Methylmercury concentrations in shellfish collected by ADEC throughout Alaska (1996-2000).[1]

Species	Number of samples	Concentration range (µg/g, ppm) wet wt.	Average concentration (ppm) wet wt.	Number of detected values
Alta razor clam	3	ND	--	0
Bairdi Tanner crab	9	0.030 - 0.086	0.045	9
Butter clam	3	ND	--	0
Cockle clam	3	ND	--	0
Dungeness crab	9	0.026-0.16	0.086	9
Geoduck clam	3	<0.025-0.025	--	1
Horse clam	3	ND	--	0
King crab	8	0.026-0.052	0.041	8
Littleneck clam	4	ND	--	0
Mussel	4	ND	--	0
Opilio Tanner crab	8	0.037-0.069	0.053	8
Oyster	5	<0.025-0.028	--	1
Razor clam	3	ND	--	0
Red neck clam	3	ND	--	0
Scallop	5	ND	--	0
Sidestrip Shrimp	2	ND	--	0
Softshell clam	2	ND	--	0
Spot Shrimp	1	0.093	--	1

[1]Source (ADEC 2002)
ND = not detected (<0.025 ppm)

Table 3: Published studies that examined total mercury (Hg) and methylmercury (MeHg) in Alaska marine mammal tissues (µg/g, ppm, wet weight).

Reference	Date Collected	Animal	Tissue[1]	Mean Hg	SD Hg	Hg N	Mean MeHg	SD MeHg	MeHg N	% MeHg
Alaska										
Becker et al. 2000	1989	Beluga Whale	L-male	3.5		1	0.49		1	14
		Beluga Whale	L-female	5.5	4.4	3	0.51	0.23	3	9.3
Becker et al. 2000	1990	Beluga Whale	L-male	36	17	3	1.5	0.59	3	4.1
		Beluga Whale	L-female	53	23	3	1.15	0.39	3	2.2
Becker et al. 2000	1992-1995	Beluga Whale	L-male	5.4	3.5	6	1.5	0.66	6	27
		Beluga Whale	L-female	2.6	1.8	4	0.52	0.25	4	20
Behlke et al. 1996	1989-95	Beluga Whale	L				0.97	0.62	16	
Woshner et al. 2001a	1992-96	Beluga Whale	L	23	26	24	1.7	0.88	24	7.4
Woshner et al. 2001a	1992-96	Beluga Whale	K	5.0	3.9	24	0.59	0.35	23	12
Woshner et al. 2001a	1992-96	Beluga Whale	M	1.2	0.83	11	1.1	0.54	24	91.7
Woshner et al. 2001a	1992-96	Beluga Whale	E	0.60	0.32	11	0.67	0.46	15	111
Becker et al. 1995	1989-93	Ringed Seal	L	2.0	2.0	9	0.41	0.23	4	21
Woshner et al. 2001b	1995-97	Ringed Seal	L	3.5	5.1	16	0.15	0.06	16	4.3
Woshner et al. 2001b	1995-97	Polar Bears	L	14	13	24	0.49	0.42	24	3.5
Woshner et al. 2001b	1995-97	Polar Bears	M	0.09	0.07	23	0.07	0.05	23	78

[1]L, liver; K, kidney; M, muscle; E, Epidermis; N, number of samples; SD, standard deviation; ww, wet weight.

Table 4: Published studies on total mercury (Hg) tissue concentrations and estimated methylmercury (MeHg) concentrations in Alaska marine mammals (µg/g, ppm, wet weight).

Reference	Date Collected	Animal	Tissue[1]	Mean Hg	SD Hg	Hg N	Estimated MeHg [2]
Galster 1971		Bearded Seal	L	1.9	1.2	4	0.19
Becker et al. 1995	1989-93	Bearded Seal	L	4.2	4.6	3	0.42
Galster 1971		Bearded Seal	M	0.20	0.15	7	0.20
Woshner et al. 2001a	1992-96	Beluga Whale	B	0.03	0.035	11	0.03
Byrne et al. 1985	1979-80	Bowhead Whale	B	0.007	0.007	7	0.007
Woshner et al. 2001a	1983-90	Bowhead Whale	B	0.002	0.007	30	0.002
Bratton et al. 1990	1986	Bowhead Whale	B	0.003	0.005	6	0.003
Byrne et al. 1985	1979-80	Bowhead Whale	K	0.006	0.006	2	0.0006
Woshner et al. 2001a	1983-90	Bowhead Whale	K	0.038	0.033	47	0.0038
Bratton et al. 1990	1986	Bowhead Whale	K	0.005	0.001	6	0.0005
Bratton et al. 1990	1988	Bowhead Whale	K	0.007	0.001	4	0.0007
Byrne et al. 1985	1979-80	Bowhead Whale	L	0.005	0.005	2	0.0005
Woshner et al. 2001a	1983-90	Bowhead Whale	L	0.060	0.073	55	0.0060
Bratton et al. 1990	1986	Bowhead Whale	L	0.008	0.001	6	0.0008
Bratton et al. 1990	1988	Bowhead Whale	L	0.007	0.001	4	0.0007
Becker et al. 1995	1992-93	Bowhead Whale	L	0.17	0.11	3	0.017
Byrne et al. 1985	1979-80	Bowhead Whale	M	0.001	0.001	2	0.001
Woshner et al. 2001a	1983-90	Bowhead Whale	M	0.017	0.011	35	0.017
Bratton et al. 1990	1986	Bowhead Whale	M	0.003	0.001	6	0.003
Bratton et al. 1990	1988	Bowhead Whale	M	0.002		1	0.002
Anas 1974	1971	Harbor Seal	L	4.2	4.2	3	0.42
Miles et al. 1992	1976-78	Harbor Seal	L	5.0	5.0	23	0.50
Goldblatt et al. 1983	1975	Northern Fur Seal	L	11	6.5	37	1.1
Galster 1971		Pacific Walrus	L	0.49	0.10	7	0.049
Taylor et al. 1989	1981-84	Pacific Walrus	L	1.5	3.2	62	0.15
Galster 1971		Pacific Walrus	M	0.020	0.005	6	0.020
Lentfer 1976	1972	Polar Bear	L	4.8	1.5	9	0.48
Lentfer 1976	1972	Polar Bear	L	3.9	1.3	16	0.39
Lentfer 1976	1972	Polar Bear	M	0.040	0.014	12	0.04
Lentfer 1976	1972	Polar Bear	M	0.040	0.26	4	0.04
Demilralp et al. 1995	1993	Ringed Seal	L	1.3	1.9	4	0.13
Woshner et al. 2001b	1995-97	Ringed Seals	B	0.002	0.001	11	0.002
Woshner et al. 2001b	1995-97	Ringed Seals	K	0.5	0.28	16	0.05
Woshner et al. 2001b	1995-97	Ringed Seals	M	0.22	0.33	11	0.22

[1]B, blubber; K, kidney; L, liver; M, muscle; N, number of samples; SD, standard deviation; ww, wet weight.

[2]Methylmercury concentrations were conservatively estimated using 10% the total mercury concentration for liver and kidney tissues and 100% for epidermis, blubber, and muscle (Woshener et al 2001a; 2001b; Wagemann et al. 1998).

Table 5. Summary of risk assessments for methylmercury (NRC 2000).

Agency	Primary Study	End Point	Biomarker and Exposure Level	Derived Intake Level µg/kg/day		Uncertainty factor	Acceptable Intake Level µg/kg/day	
USEPA	Faroe Islands (Grandjean et al. 1997)	Developmental neurotoxicity measured by neuropsychological tests	Cord blood = 58 µg/L	BMDL	1.1	10	RfD	0.1
ATSDR	Seychelles Islands (Davidson et al. 1998)	Developmental neurotoxicity measured by neuropsychological tests	Mean maternal hair level (highest exposure group) = 15.3 ppm	NOAEL	1.3	4.5	MRL	0.3
JECFA (FAO/WHO)	Seychelles Islands (Davison et al. 1998); Faroe Islands (Grandjean et al. 1997)	Developmental neurotoxicity measured by neuropsychological tests	Maternal hair = 14 ppm	NOEL	1.5	6.4	PTDI	0.2 (WBCA)
	Japanese data (Friberg et al. 1971)	Overt neurological symptoms in adults	Adult blood = 0.2 ppm	LOAEL	4.3	10	PTDI	0.5 (other adults)
FDA	Japanese data (Friberg et al. 1971)	Overt neurological symptoms in adults	Adult blood = 0.2 ppm	LOAEL	4.3	10	Action level in fish, 1ppm	0.5
Health Canada	Seychelles Islands (Davison et al. 1998); Faroe Islands (Grandjean et al. 1997); New Zealand (Kjellstrom 1986, 1989)	Developmental neurotoxicity	Maternal hair = 10 ppm	Benchmark dose	1	5	PTDI	0.2 (child and WCBA) 0.5 (all other adults)

USEPA = United States Environmental Protection Agency
ATSDR = Agency for Toxic Substances and Disease Registry
JECFA = Joint FAO/WHO Expert Committee on Food Additives
FDA = Food and Drug Administration
WCBA = Women of childbearing age
BMDL = Benchmark Dose (lower 95% confidence limit)
NOAEL = No Observed Adverse Effect Level
LOAEL = Lowest Observed Adverse Effect Level
RfD = Reference Dose
MRL = Minimal Risk Level
PTDI = Provisional Tolerable Daily Intake

Table 6. Five fish species most frequently harvested by subsistence region. Reported by the Department of Fish and Game Division of Subsistence (ADFG 2001).

Region	Resource	Per Capita Edible Pounds Harvested for Each Resource	Percentage (by weight) of Total Harvest for Each Resource
Arctic	Sheefish	70.47	12.71%
	Arctic Cisco	57.16	10.31%
	Chum Salmon	46.61	8.40%
	Dolly Varden	30.39	5.48%
	Whitefish	28.37	5.12%
Interior	Summer Chum	278.00	51.28%
	Fall Chum	200.50	36.98%
	Chinook Salmon	53.29	9.83%
	Whitefish	39.70	7.32%
	Chum Salmon	36.09	6.66%
Southcentral	Halibut	17.73	15.21%
	Sockeye Salmon	16.58	14.22%
	Coho Salmon	12.35	10.59%
	Chinook Salmon	10.79	9.25%
	Trout	3.47	2.98%
Southeast	Halibut	24.95	11.89%
	Chinook Salmon	18.14	8.65%
	Sockeye Salmon	18.13	8.64%
	Coho Salmon	14.75	7.03%
	Herring Roe on Hemlock Branches	7.30	3.48%
Southwest	Sockeye Salmon	52.33	20.56%
	Halibut	37.26	14.64%
	Spawnouts	32.13	12.63%
	Coho Salmon	22.51	8.84%
	Spawning Sockeye	20.07	7.89%
Western	Herring	138.68	15.94%
	Chinook Salmon	130.48	15.00%
	Chum Salmon	127.19	14.62%
	Blackfish	60.61	6.97%
	Sockeye Salmon	57.36	6.60%

Table 7. Five marine mammals most frequently harvested by subsistence region. Reported by the Department of Fish and Game Division of Subsistence (ADFG 2001).

Region	Resource	Per Capita Edible Pounds Harvested for Each Resource	Percentage (by weight) of Total Harvest for Each Resource
Arctic	Bearded Seal	227.96	41.11%
	Bowhead	72.55	13.08%
	Walrus	32.09	5.79%
	Ringed Seal	16.69	3.01%
	Beluga	14.37	2.59%
Southcentral	Harbor Seal	4.77	4.09%
	Steller Sea Lion	0.34	0.29%
	Porpoise	0.10	0.09%
	Beluga	0.05	0.04%
Southeast	Harbor Seal	12.01	5.72%
	Sea Otter	0.16	0.08%
	Steller Sea Lion	0.02	0.01%
Southwest	Fur Seal	58.7	23.06%
	Harbor Seal	11.12	4.37%
	Steller Sea Lion	4.93	1.94%
	Beluga	2.99	1.17%
	Minke (bottlenose)	1.33	0.52%
Western	Bearded Seal	30.62	3.52%
	Beluga	22.56	2.59%
	Ringed Seal	21.63	2.49%
	Seal	19.68	2.26%
	Spotted Seal	17.24	1.98%

Table 8. Rank Order of Species Harvested in Alaska (1992-2002). Alaska Department of Fish and Game, Division of Commercial Fisheries and National Marine Fishery Service (ADFG 2002).

Species	Average pounds harvested per year
Pollock, walleye	2.75E+09
Cod, Pacific gray	5.54E+08
Salmon, pink	2.95E+08
Sole, Yellow fin	2.12E+08
Salmon, Sockeye	1.65E+08
Crab, Tanner, opilio	1.46E+08
Salmon, chum	1.35E+08
Greenling, atka mackerel	1.31E+08
Herring	9.78E+07
Sole, rock	6.37E+07
Halibut	6.35E+07
Sablefish, blackcod	4.44E+07
Salmon, coho	3.46E+07
Perch, Pacific Ocean	3.78E+07
Sole, flathead	2.33E+07
Crab, Tanner, bairdi	1.01E+07
Flounder, arrowtooth	1.11E+07
Crab, red king	9.70E+06
Salmon, Chinook	7.65E+06
Crab, brown king	6.93E+06
Crab, Dungeness	4.67E+06
Skate, general	4.22E+06
Crab, blue king	2.65E+06
Shrimp, pink	2.20E+06
Urchin, red	2.12E+06
Sea cucumber	1.37E+06

Table 9. Allowable routine weekly intake of seafood (in pounds) by an average weight 67 kg woman of reproductive age based upon varying concentrations of Hg in seafood and agency guidelines.

	USEPA-WCBA		WHO-WCBA		WHO-Adult	
	RfD (BMDL/10)	**Critical end-point** (BMDL)	**PTDI** (NOEL/6.4)	**Critical endpoint** (NOEL)	**PTDI** (LOAEL/10)	**Critical endpoint** (LOAEL)
Daily dose of methylmercury (µg/kg/day)	0.1	1.0	0.2	1.5	0.5	5
Seafood Hg concentration (ppm)						
0.01[a]	10	100	20	128	52	520
0.05[b,c]	2.1	21	4.2	27	10	100
0.25[d,e]	0.41	4.1	0.82	5.2	2.1	21
0.50[f,g]	0.21	2.1	0.42	2.7	1.0	10
1.0[h,i]	0.10	1.0	0.20	1.3	0.5 2	5.2

a. Methylmercury in bowhead whale tissues range from 0.001 ppm to 0.017 ppm assuming methylmercury is approximately 10% of the total mercury concentration in liver and kidney tissues.

b. Average total mercury or methylmercury in Alaskan samples of clams, mussels, oyster, scallops, sidestrip shrimp, softshell clam, king crab, tanner crab, octopus, ocean perch, eelfish, pink salmon, pollock, herring, casper fish, red salmon, sole, chum salmon, rainbow trout, yellowfin sole, dover sole, silver salmon range from 0.012 ppm to 0.05 ppm.

c. Average methylmercury in Pacific Alaska walrus muscle and liver, beluga blubber, polar bear muscle, and ringed seal kidney tissues range between 0.01 ppm and 0.07 ppm assuming methylmercury is approximately 10% of the total mercury concentration in liver and kidney tissues.

d. Average total mercury or methylmercury concentrations in dungeness crab, spot shrimp, starry flounder, king salmon, black rockfish, dusky rockfish, sea bass, sablefish, tuna, gray cod, halibut, round shark, grayling, burbot, sheefish, and whitefish range from 0.05 ppm to 0.25 ppm..

e. Average methylmercury in bearded seal and ringed seal muscle tissue are less than 0.25 ppm.

f. Average total mercury or methylmercury concentrations in quillback rockfish, spiney dog fish, lingcod, tiger rockfish, yellow eye rockfish range from 0.25 ppm to 0.5 ppm.

g. Average methylmercury concentrations of ringed seal, bearded seal, harbor seal, and polar bear liver are less than 0.5 ppm assuming methylmercury is approximately 10% of the total mercury concentration in liver tissues.

h. Average total mercury or methylmercury concentrations of northern pike, and salmon shark range from 0.5 ppm to 1 ppm. Also, the high-end of values of Hg identified in older/larger marine and fresh water finfish such as lingcod, tiger rockfish, yellow eye rockfish, northern pike, and salmon shark approach or could exceed 1 ppm.

i. Average methylmercury concentrations in beluga kidney, liver, muscle and epidermis tissues approach or exceed 1 ppm.

Table 10. Selenium concentrations in Alaska marine mammals (μg/g, ppm, wet weight).

Reference	Date Collected	Animal	Tissue[1]	Mean Concentration	SD	N
Becker et al. 1995	1989-93	Bearded Seal	L	3.1	2.0	3
Woshner et al. 2001a	1992-1996	Beluga Whale	B	0.58	0.36	16
Woshner et al. 2001a	1992-1996	Beluga Whale	E	9.6	7.5	17
Woshner et al. 2001a	1992-1996	Beluga Whale	K	6.3	3.2	45
Woshner et al. 2001a	1992-1996	Beluga Whale	L	41	33	50
Becker et al. 2000	1989	Beluga Whale	L-female	8.5	5.3	3
Becker et al. 2000	1990	Beluga Whale	L-female	37	33	3
Becker et al. 2000	1992-1995	Beluga Whale	L-female	2.6	1.5	4
Becker et al. 2000	1992-1995	Beluga Whale	L-male	4.3	1.6	6
Becker et al. 2000	1989	Beluga Whale	L-male	6.2		1
Becker et al. 2000	1990	Beluga Whale	L-male	19	8.8	7
Woshner et al. 2001a	1992-1996	Beluga Whale	M	0.28	0.06	24
Woshner et al. 2001a	1983-1990	Bowhead Whale	B	0.06	0.03	38
Byrne et al. 1985	1979-80	Bowhead Whale	B	0.001	0.001	7
Bratton et al. 1990	1986	Bowhead Whale	B	0.005	0.005	6
Woshner et al. 2001a	1983-1990	Bowhead Whale	K	1.6	0.42	48
Byrne et al. 1985	1979-80	Bowhead Whale	K	0.028	0.028	2
Bratton et al. 1990	1986	Bowhead Whale	K	1.6	0.33	6
Bratton et al. 1990	1988	Bowhead Whale	K	1.8	0.20	4
Woshner et al. 2001a	1983-1990	Bowhead Whale	L	1.6	0.81	55
Byrne et al. 1985	1979-80	Bowhead Whale	L	0.080	0.080	2
Becker et al. 1995	1992-93	Bowhead Whale	L	0.91	0.40	3
Bratton et al. 1990	1986	Bowhead Whale	L	1.3	0.30	6
Bratton et al. 1990	1988	Bowhead Whale	L	1.2	0.19	4
Woshner et al. 2001a	1983-1990	Bowhead Whale	M	0.35	0.33	42
Byrne et al. 1985	1979-80	Bowhead Whale	M	0.13	0.13	2
Bratton et al. 1990	1986	Bowhead Whale	M	0.42	0.16	6
Bratton et al. 1990	1988	Bowhead Whale	M	0.47		1
Miles et al. 1992	1976-78	Harbor Seal	L	1.6	1.6	23
Taylor et al. 1989	1981-84	Pacific Walrus	K	9.5	6.3	3
Taylor et al. 1989	1981-84	Pacific Walrus	L	2.3	2.0	65
Woshner et al. 2001b	1995-1997	Polar Bears	B	0.04	0.02	11
Woshner et al. 2001b	1995-1997	Polar Bears	K	13	11	24
Woshner et al. 2001b	1995-1997	Polar Bears	L	9.3	13	24
Woshner et al. 2001b	1995-1997	Polar Bears	M	0.54	0.15	23
Becker et al. 1995	1989-93	Ringed Seal	K	3.2	3.2	2
Becker et al. 1995	1989-93	Ringed Seal	L	3.0	1.5	14
Woshner et al. 2001b	1995-1997	Ringed Seals	B	0.21	0.11	16
Woshner et al. 2001b	1995-1997	Ringed Seals	K	2.5	0.97	17
Woshner et al. 2001b	1995-1997	Ringed Seals	L	7.2	5.8	17
Woshner et al. 2001b	1995-1997	Ringed Seals	M	0.28	0.09	16

[1]B, blubber; E, epidermis; K, kidney; L, liver; M, muscle; N, number of samples; SD, standard deviation; ww, wet weight.

Table 11. Studies of human hair mercury concentrations in Alaska.

Location	Population	Hair Total Mercury (ppm) Mean	Range	N	Reference
Pribilof Islands	All Alaska Natives	4.6	1.0[a]	42	Hochberg et al.1972
	-seal liver consumption	5.6	1.7[a]	15	
	-no seal liver	4.9	2.2[a]	13	
	Non-Native-no seal liver	3.4	2.2[a]	6	
Pribilof Islands	Residents	5.8	0.3 – 13	13	ADPH 1972
Bethel	Native mothers	5.1	1.5 - 9.1	14	
Juneau	Adult males	1.5	0.7 - 2.4	8	
Y-K Delta river villages	Residents	1.2	0.0 – 2.2	56	
Y-K Delta coastal villages	Native mothers	4.3	0.6[b]	12	Galster 1976
Y-K Delta interior villages	Native mothers	3.6	0.7[b]	6	
Anchorage	Native mothers	4.0	0.8[b]	4	
Nome	Women of childbearing age	1.0	1.0[c]	200	Crecelius et al. 1990
Nome	Women of childbearing age	1.4	1.0[c]	80	Lasorsa et al. 1991
Y-K Delta village of Napakiak	Alaska Native adults	1.5[d]	1.0[c]	16	Rothschild and Duffy 2002a
Fairbanks	Non-Native adults	0.19[d]	0.12[c]	20	
Y-K Delta Villages	Pregnant women	1.1	0.35-1.9	6	ADPH 2002a
North Slope Villages	Pregnant women	0.60	0.29-1.1	3	
Alaska Maternal Hair Mercury Biomonitoring Program	Pregnant women	0.71	0.02-6.35	176	ADPH 2004
	Women of childbearing age	1.2	0.15-8.36	60	

[a]95% confidence limit
[b]standard error
[c]standard deviation
[d]methylmercury concentration

Table 12. Mercury concentrations in maternal blood from circumpolar countries [geometric mean (range) μg/L, ppb, whole blood]. From AMAP 2003.

Country / Ethnic Group / Region	N	Mercury (total)	Mercury (organic)
Canada			
Caucasian (1994-99)	134	0.9 (nd-4.2)	0.69 (nd-3.6)
Metis/Dene (1994-99)	92	1.4 (nd–6.0)	0.80 (nd-4.0)
Other (1995)	13	1.3 (0.20–3.4)	1.2 (nd-3.0)
Inuit			
Baffin (1996)	31	6.7 (nd-34)	6.0 (nd-29)
Inuvik (1998-99)	31	2.1 (0.60-24)	1.8 (nd-21)
Kitikmeot (1994-95)	63	3.4 (nd-13)	2.9 (nd-11)
Kivalliq (1996-97)	17	3.7 (0.60-12)	2.7 (0.40-9.7)
Nunavik (1995-2000)	162	9.8 (1.6-44)	na
Greenland			
Disko Bay (1997)	94	na	na
Thule (1997)	4	50[1]	na
Ilullissat (1999-2000)	29	12.4	na
Nuuk (1999)	34	3.6	na
Ittoqqortoormiit (1999-2000)	8	10.5	na
Alaska[2]			
Bethel (2002)	52	6.5 (0.6-21)	na
Barrow (2002)	29	1.5[1] (0.0-4.5)	na
Siberian Russia			
Non-indigenous			
Norilsk (1995-96)	49	1.4 (1-5)	na
Salekhard (1996-98)	31	1.5 (1-5)	na
Dudinka (1995-96)	27	1.6 (1-5)	na
Indigenous			
Taymir (1995-96)	18	2.7 (2-8)	na
Yamal (1996-98)	12	2.9 (2-7)	na
Finland (1996-98)	130	1.4 (0.2-6.0)	na
Faroe Islands (2000-2001)	124	1.2 (nd-7.5)	na

nd = not detected
na = not available
[1]arithmetic mean
[2]Berner (2003) personal communication

Figure 1. Cycling of Mercury in an Aquatic System. CH_3Hg+, Methylmercury Ion; CH_3HgCH_3, Dimethylmercury; Hg(II), Mercuric Mercury; Hg^0, Elemental Mercury; H_2S, Hydrogen Sulfide; HgS, Cinnabar. Source: Adapted From NRC (2000).

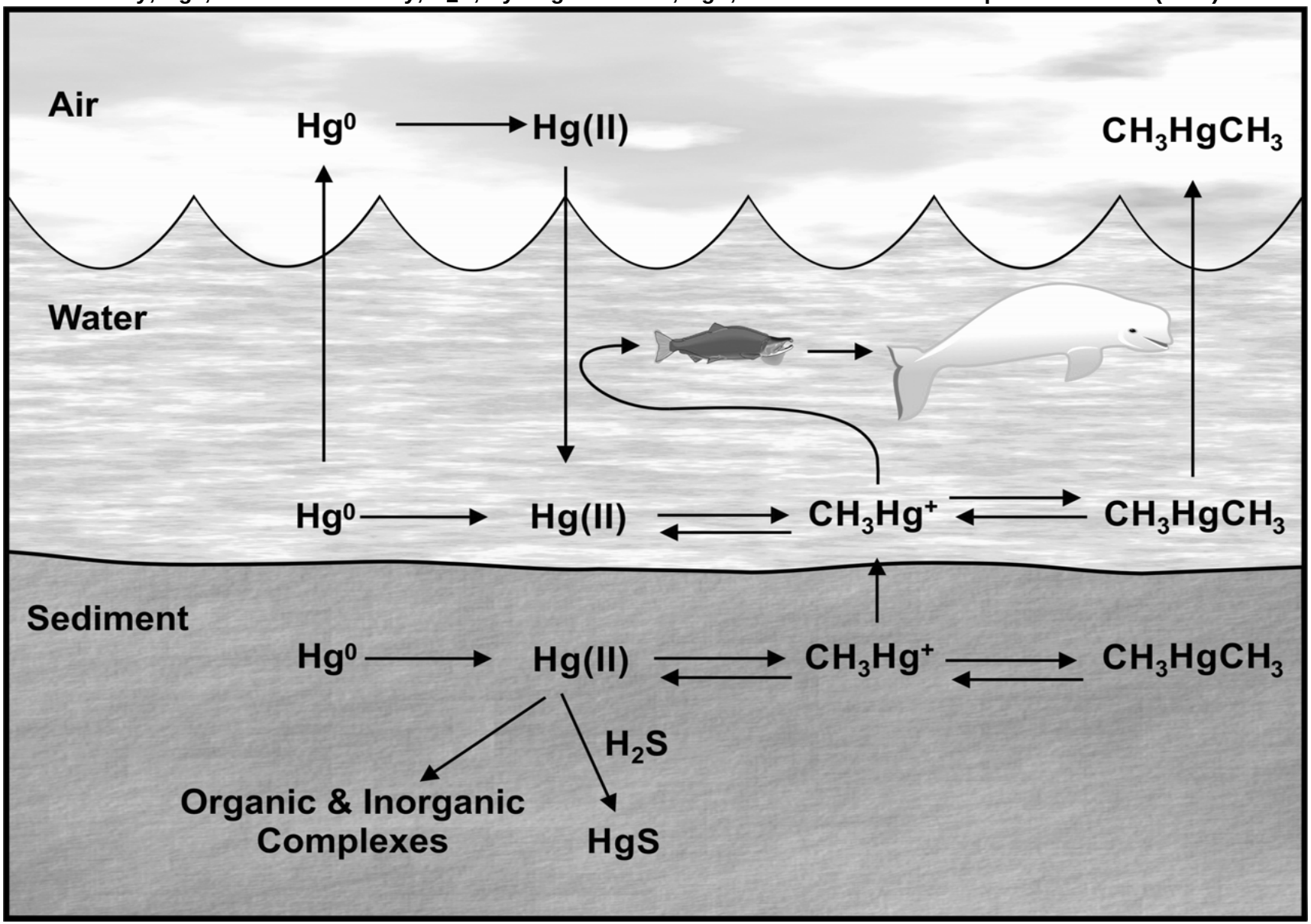


Figure 2. ADEC (2002) Cook Inlet Fish Collected in 1997-2001.

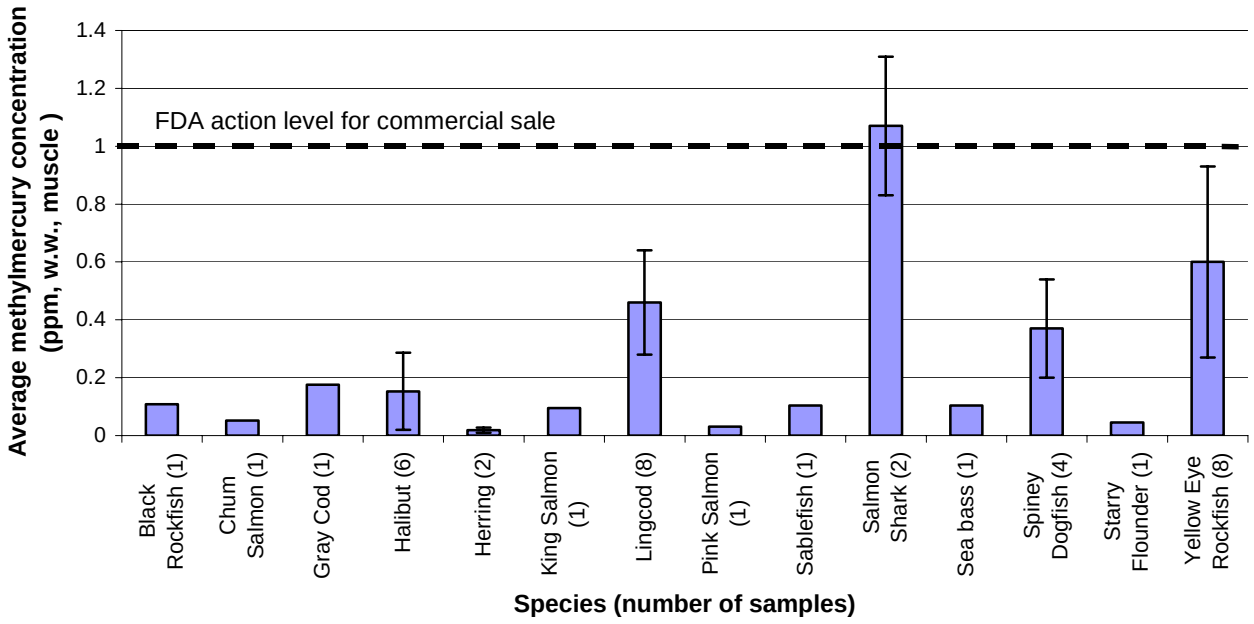


Figure 3. USEPA (2001) Cook Inlet Fish Collected in 1999.

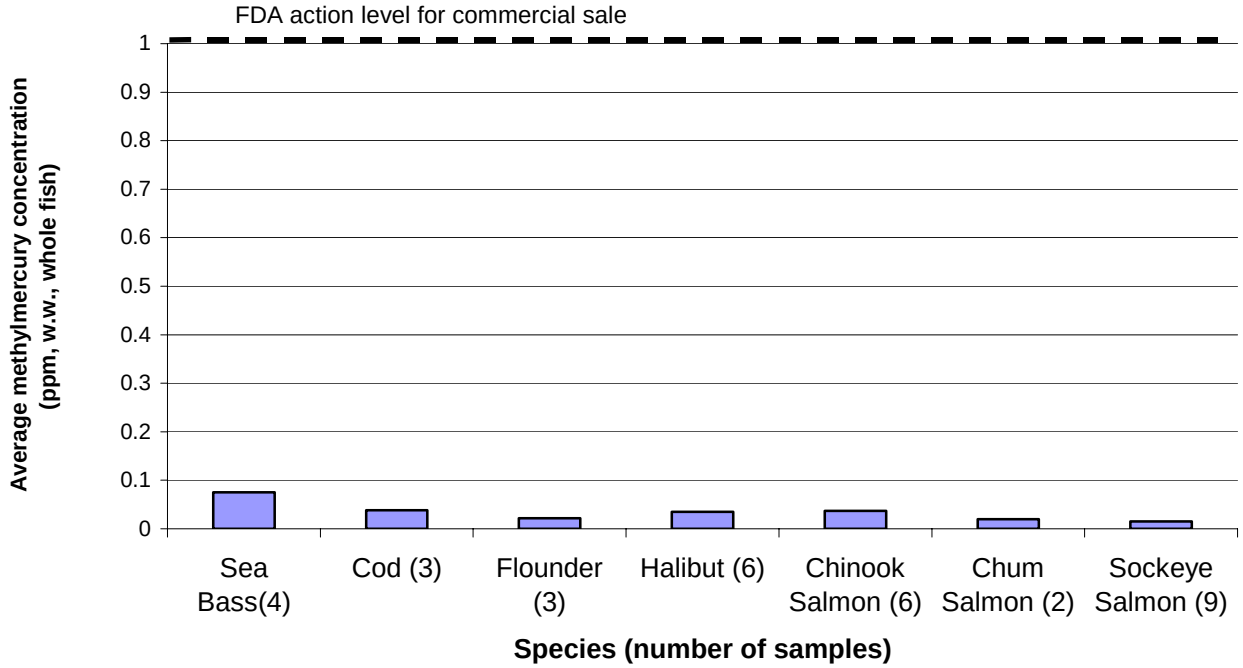


Figure 4. ADEC (2002) Prince William Sound Fish Collected in 1997-2001.

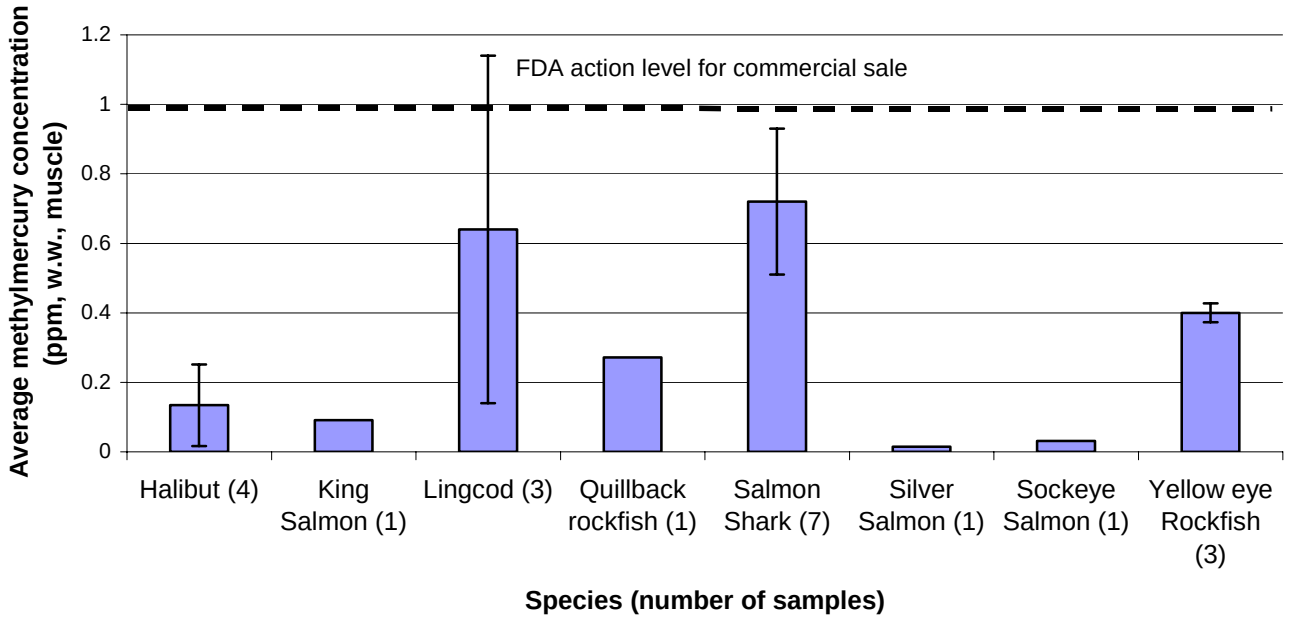


Figure 5. ADEC (2002) Southeast Marine Waters Fish Collected in 1997-2001.

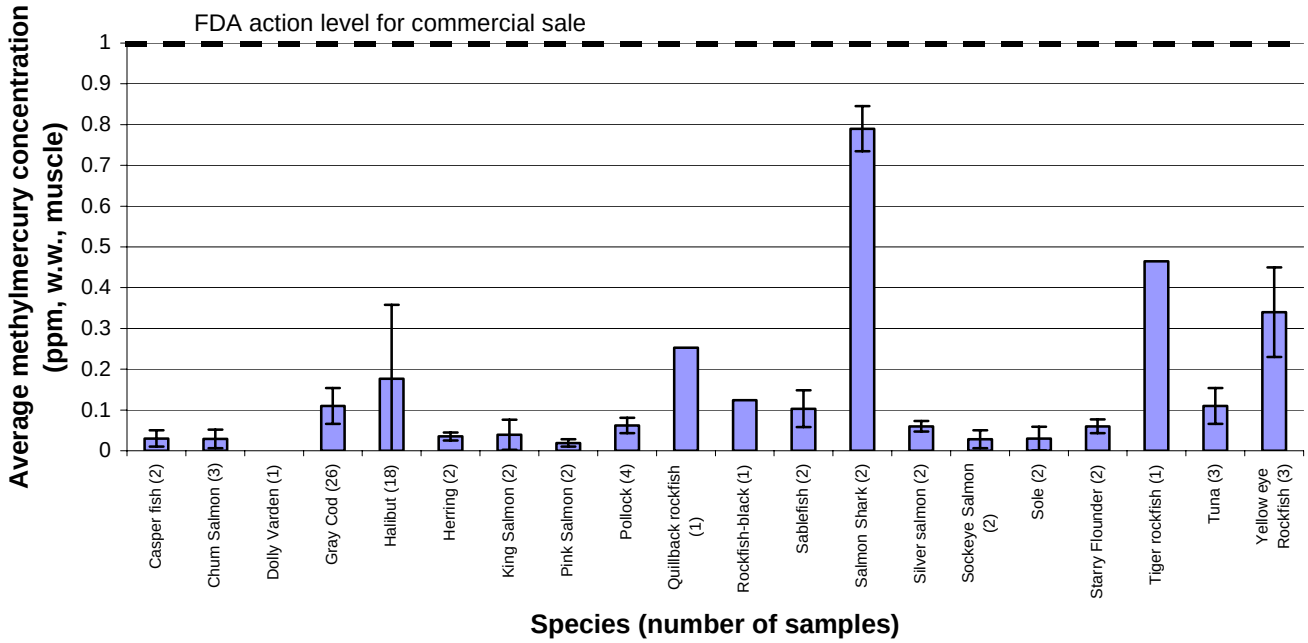


Figure 6. ADEC (2002) Aleutian and Bering Sea Fish Collected in 1997-2001.

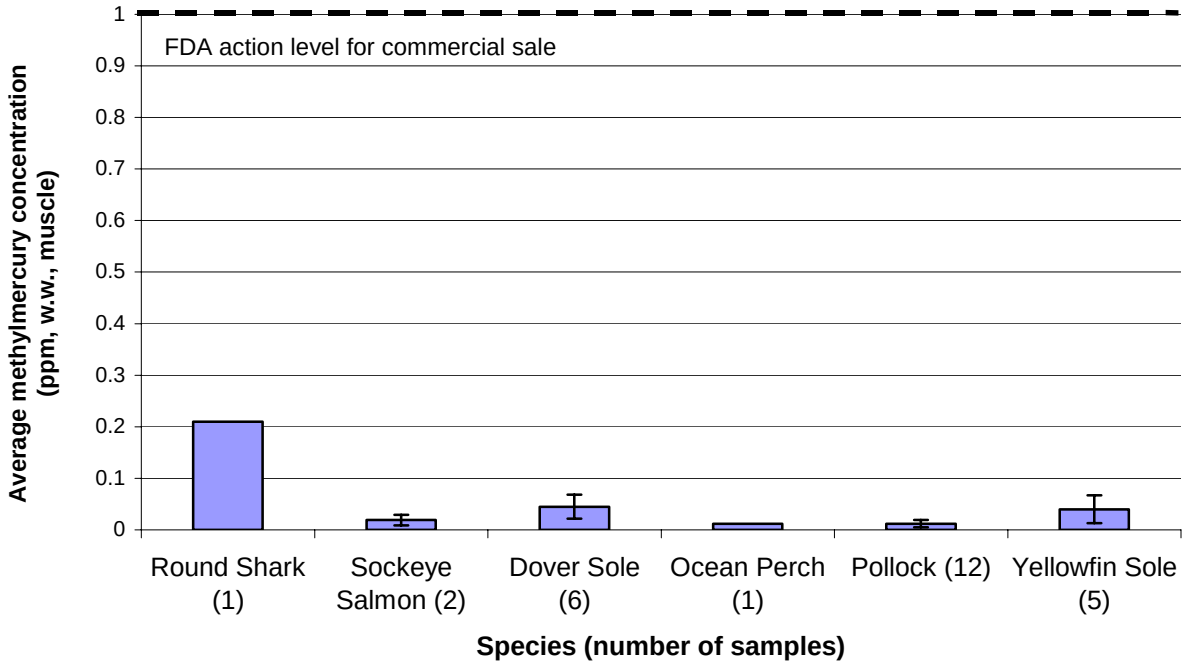


Figure 7. ADEC (2003) Salmon Data Collected in 2002.

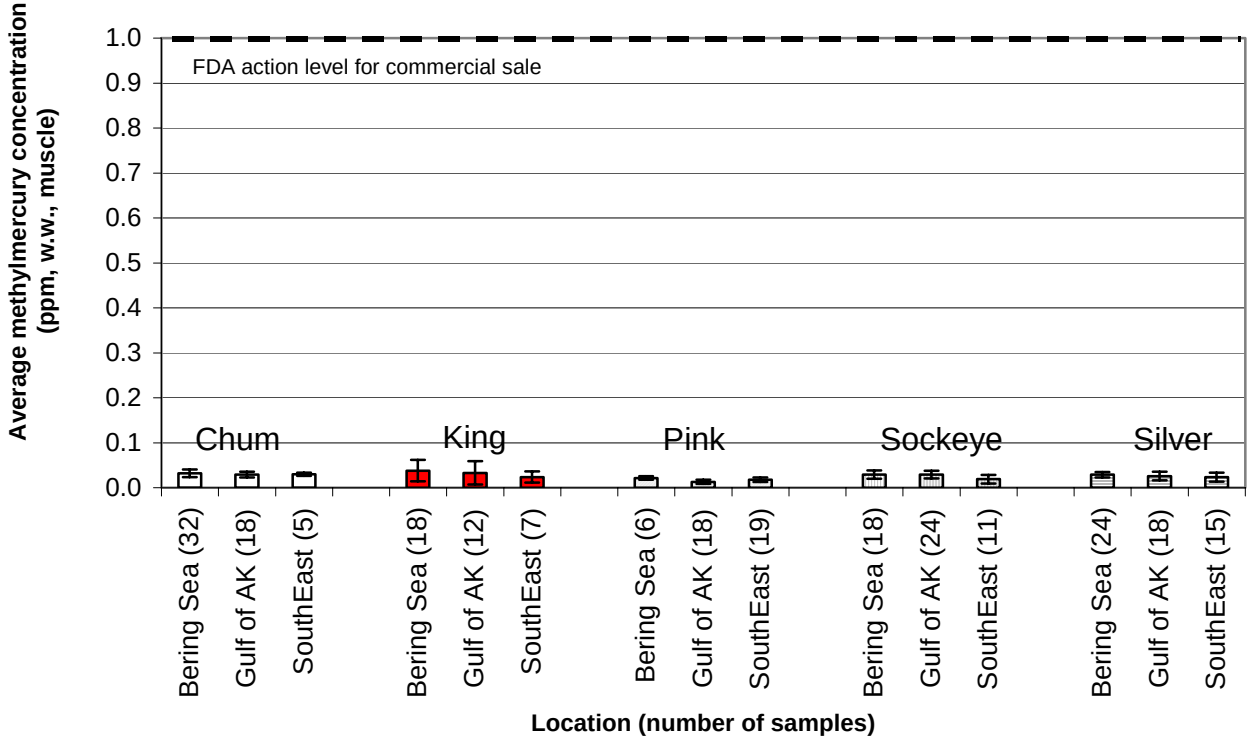


Figure 8a. Methylmercury Concentrations in Alaska Salmon Collected from Freshwater (Zhang et al. 2001; n = 6 unless noted otherwise).

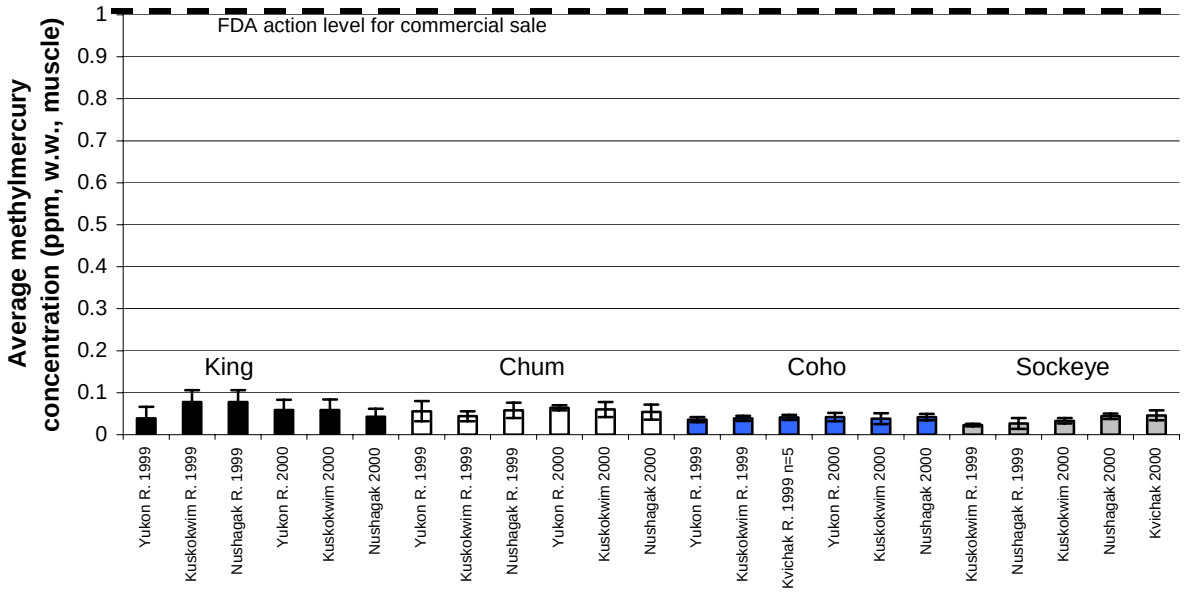
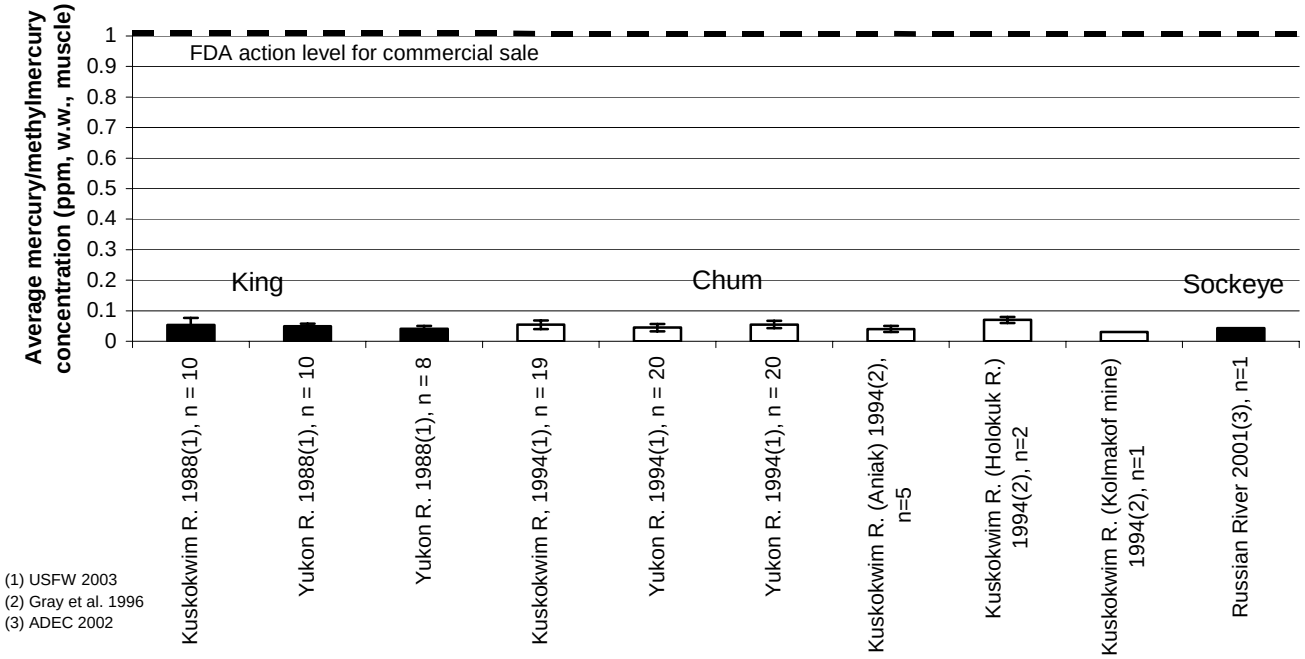


Figure 8b. Mercury/methylmercury Concentrations in Alaskan Salmon Collected from Freshwater.



(1) USFW 2003
(2) Gray et al. 1996
(3) ADEC 2002

Figure 9. ADEC (2003) Groundfish Data Collected in 2002.

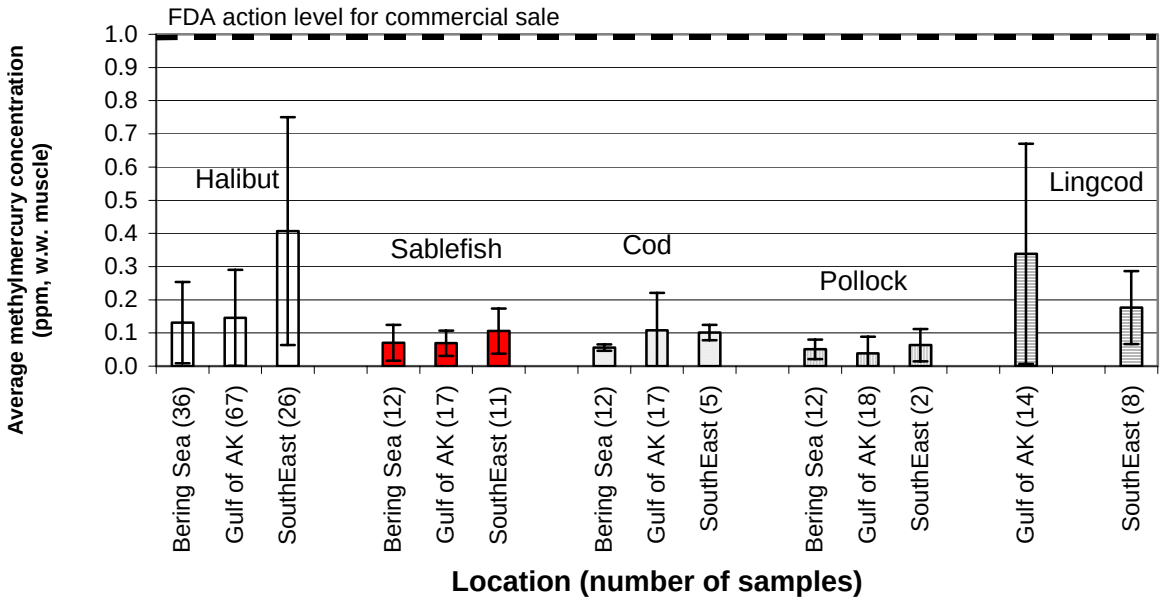


Figure 10. Pacific Halibut Collected in 1975 (Hall et al. 1976).

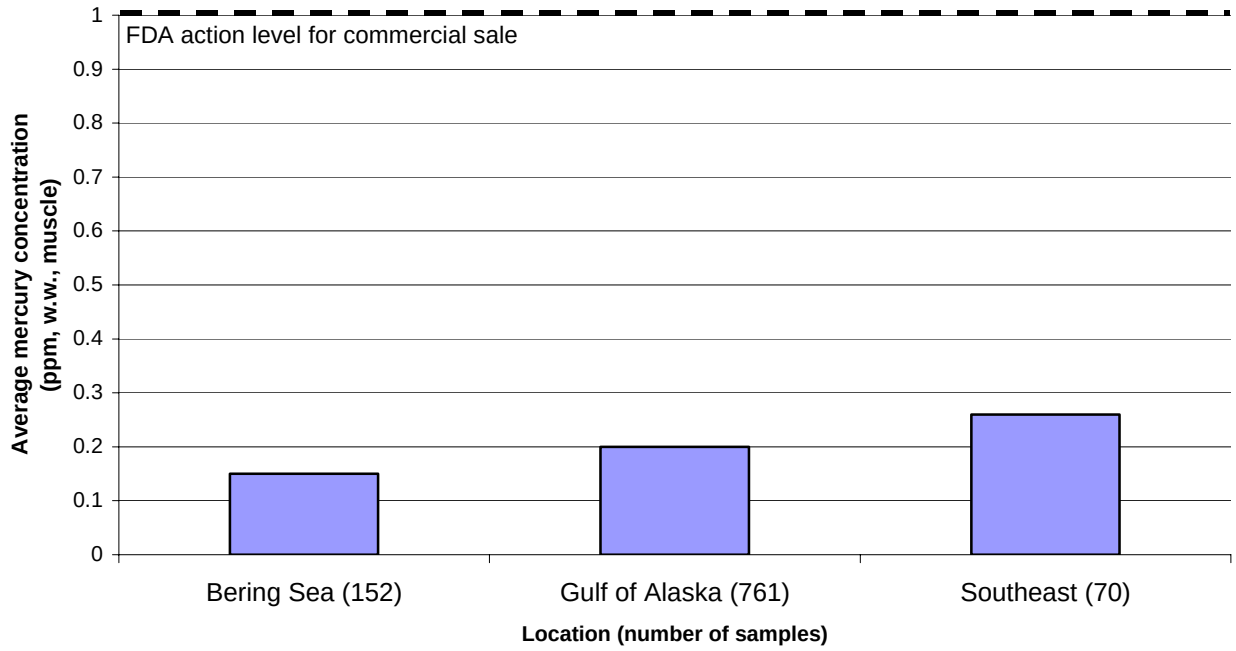


Figure 11. ADEC (2002) Kodiak Marine Waters Fish Collected in 1997-2001.

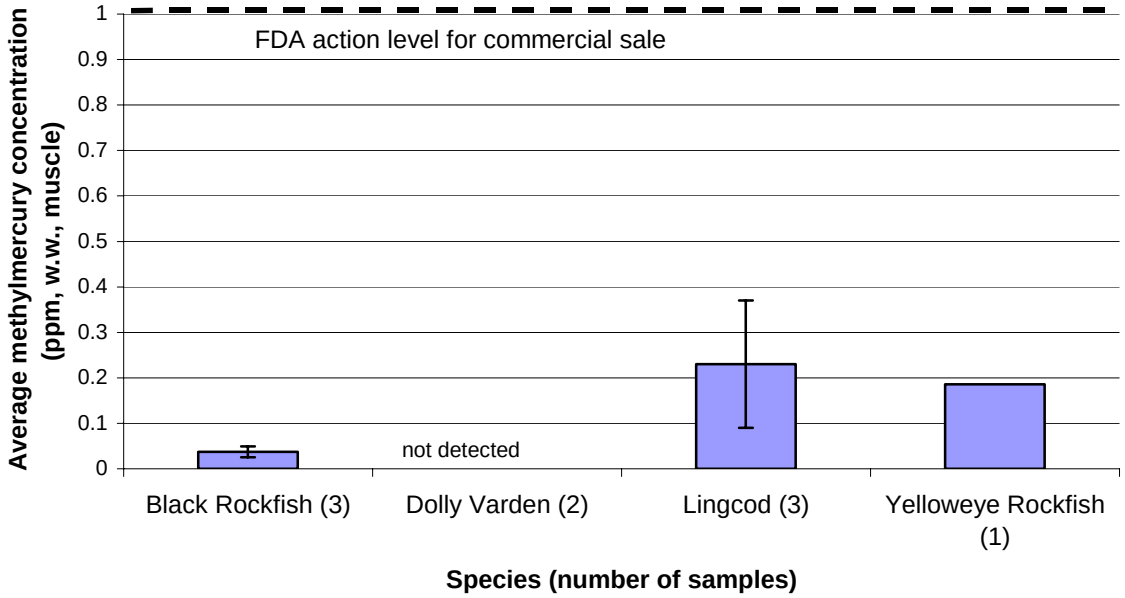


Figure 12. ADEC (2003) Rockfish Data Collected in 2002.

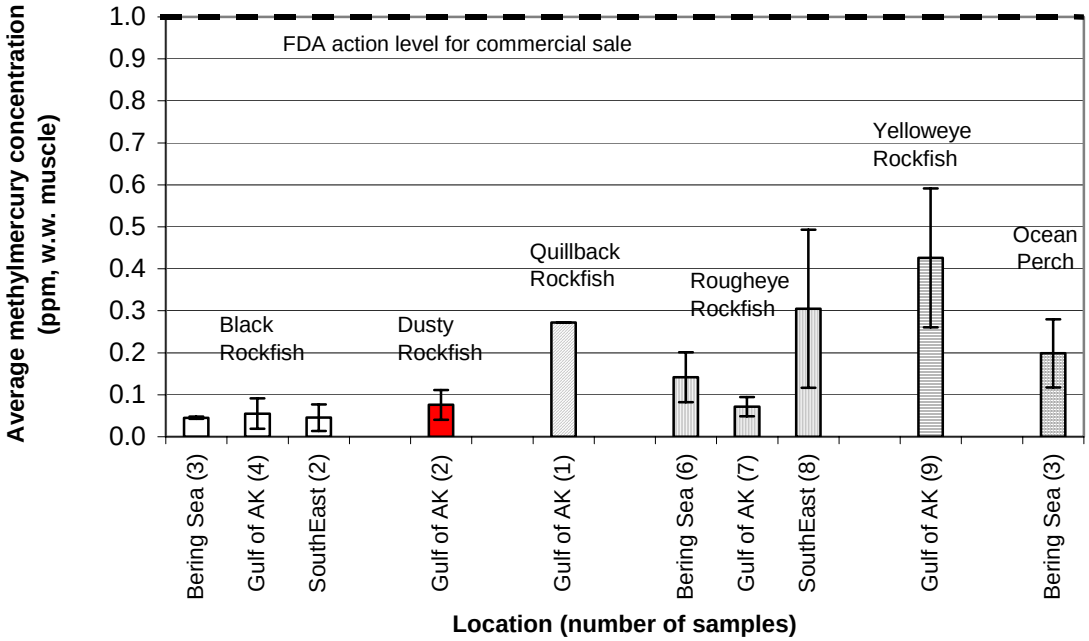


Figure 13. Alaskan Freshwater Fish Mercury Concentrations.

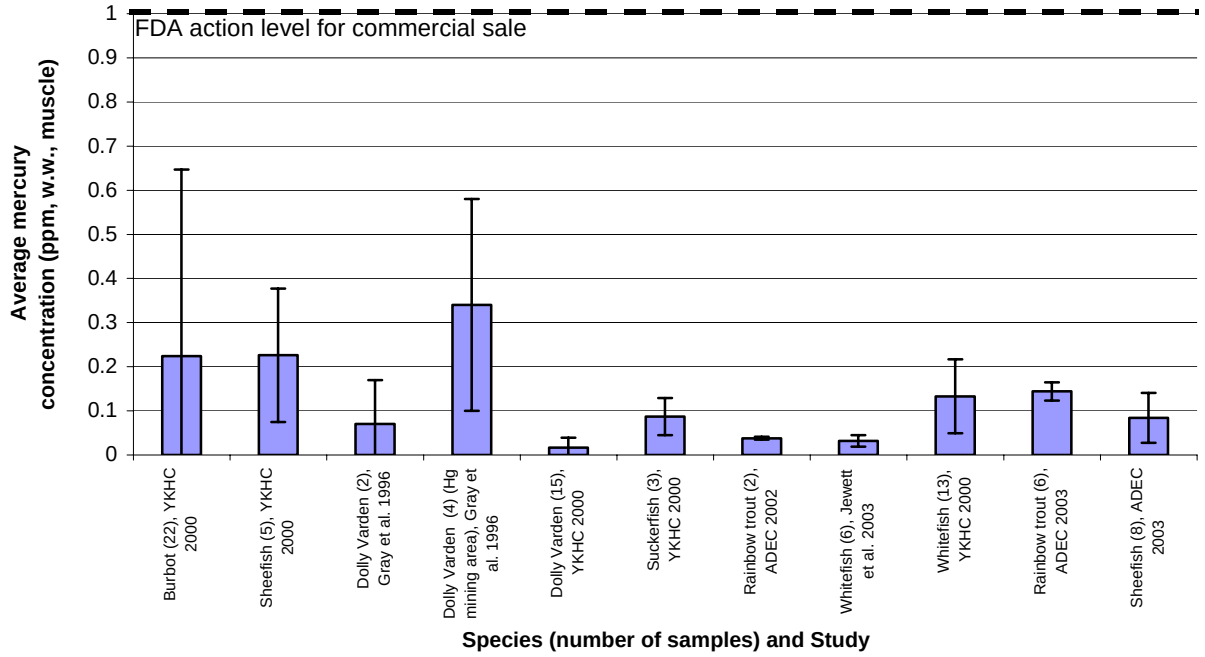


Figure 14. Alaskan Arctic Grayling Mercury Concentrations.

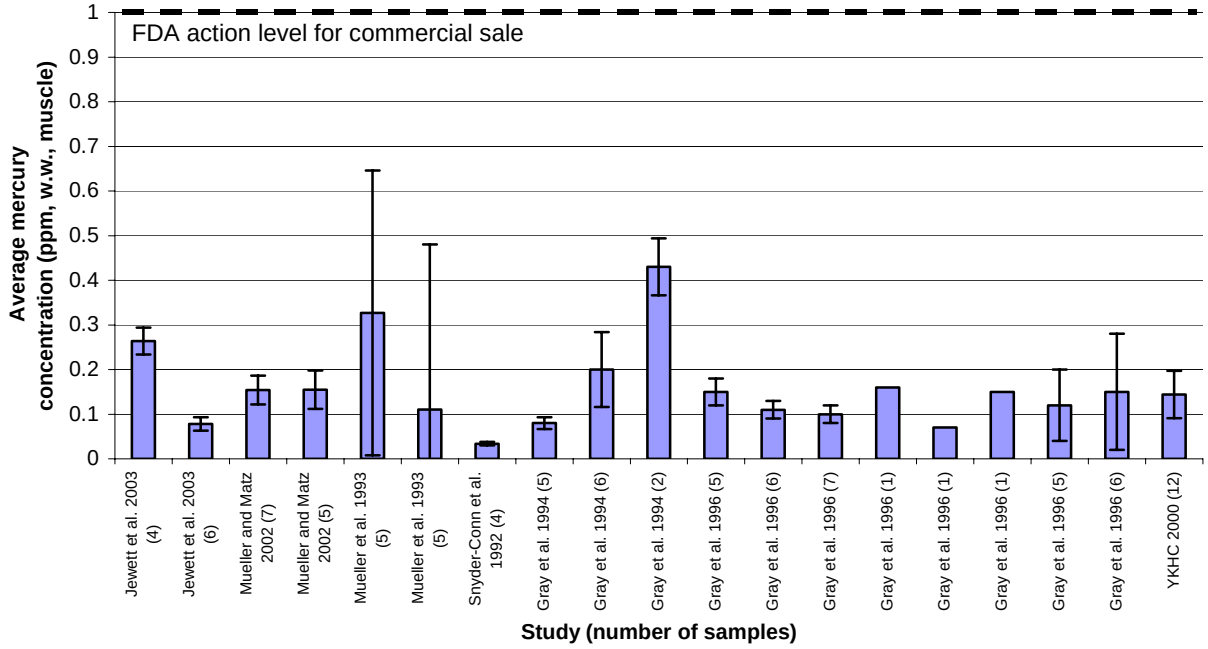


Figure 15. Alaskan Northern Pike Mercury Concentrations.

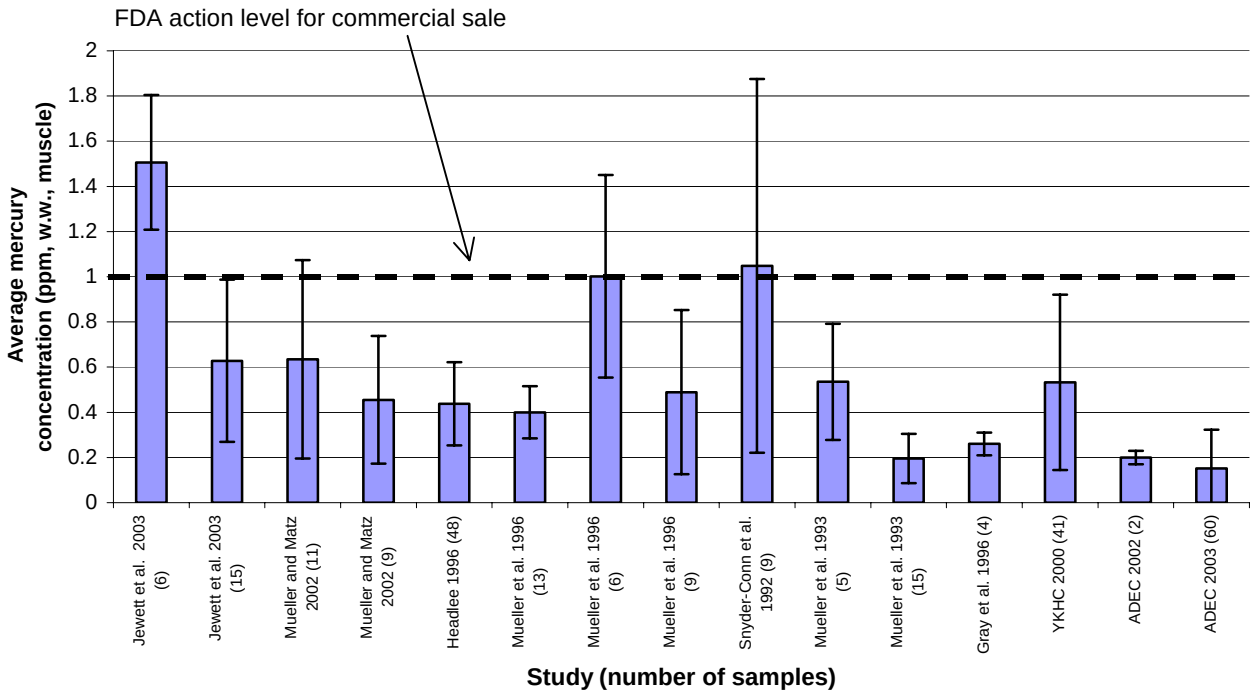
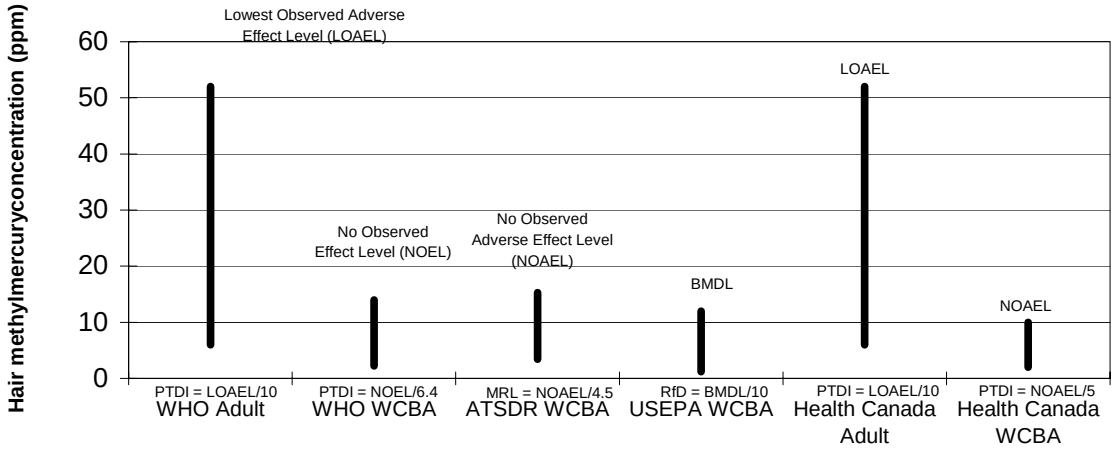


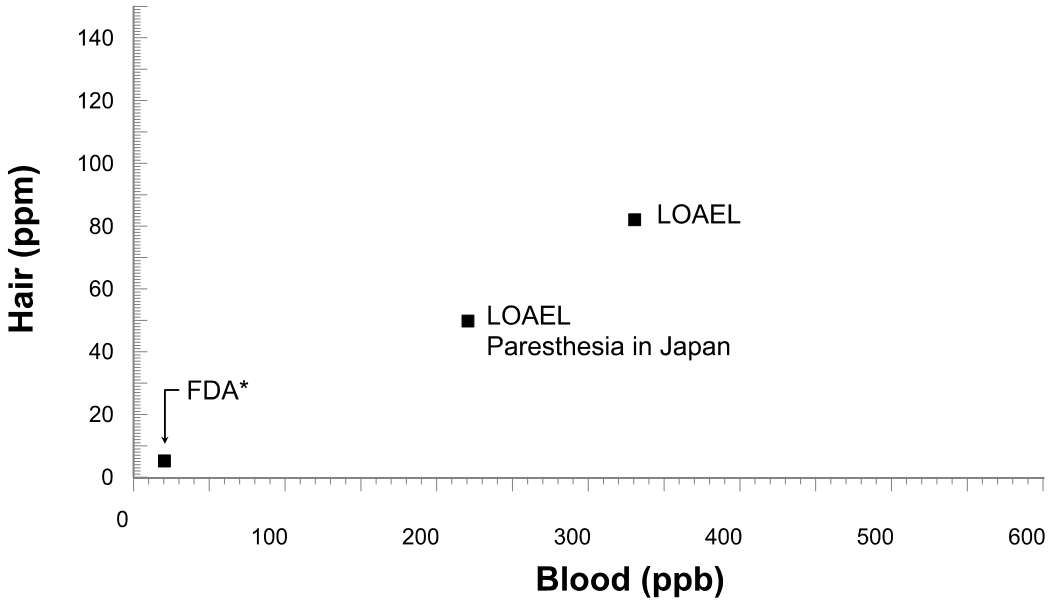
Figure 16. Agency Hair Methylmercury Guidelines Indicating the Critical Dose and Associated Uncertainty Factors.



PTDI = Provisional Tolerable Daily Intake
BMDL = Benchmark Dose (lower 95% confidence limit)
RfD = Reference Dose
MRL = Minimal Risk Level
WCBA = Women of Childbearing Age

WHO = World Health Organization
ATSDR = Agency for Toxic Substances and Disease Registry
USEPA = United States Environmental Protection Agency

Figure 17. Lowest Observed Adverse Effect Level (LOAEL) of Methylmercury in Adults Based Upon Paresthesia in Japan.



***** The LOAEL was paresthesia in an adult at hair mercury concentrations of 52 ppm. Current FDA and WHO guidelines incorporate a margin of safety with hair concentrations of 5-6 ppm and blood concentrations of 20 ppb being recommended as allowable exposures. These values correspond to the WHO Provisional Tolerable Weekly Intake for the average weight, 70-kg, adult which is 230 µg for methylmercury or 300 µg for total Hg, or a calculated dietary intake of 0.5 µg/kg/day. Source: (Tollefson et al. 1986; WHO 1990).

Hair of the individual with paresthesia at the lowest hair concentration observed (52 ppm) was reanalyzed using the atomic absorption analytic technique. The reanalyses provided a higher hair concentration (86 ppm) than what was previously measured. Source: (WHO 1990).

Figure 18. The Regional Composition of Subsistence Resources in Alaska.

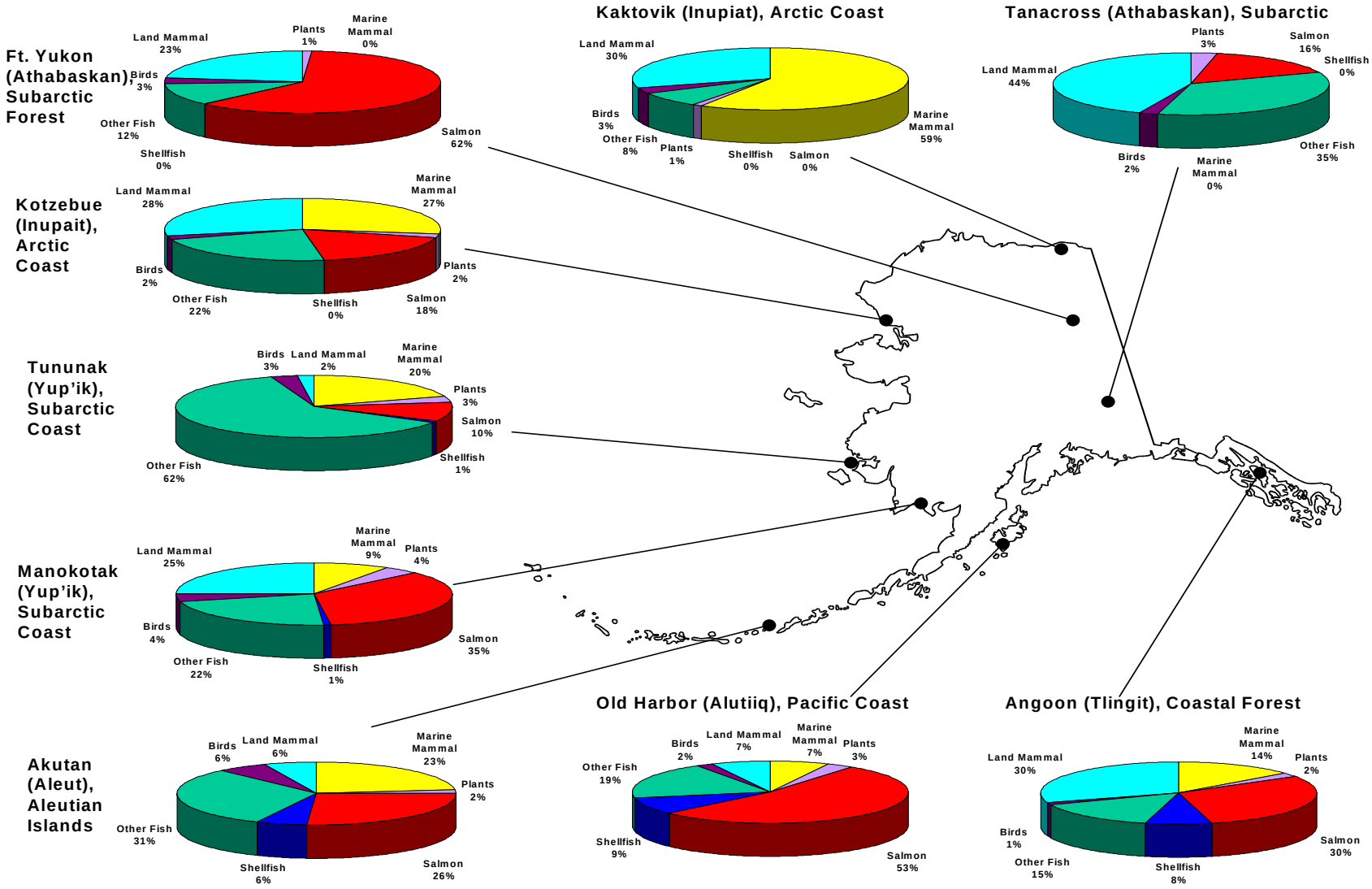


Figure 19. The Community Residence (n = 39) of Pregnant Women (n = 177) and Women of Childbearing Age (n = 60) Who Participated in the Statewide Maternal Hair Mercury Biomonitoring Program.

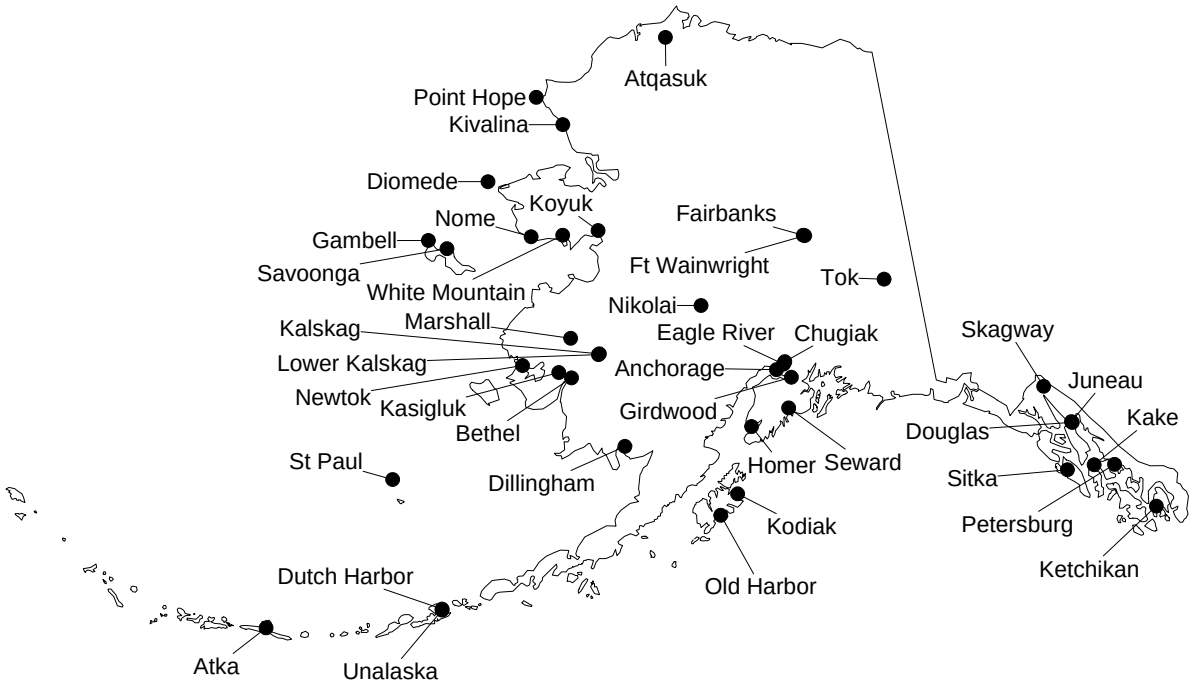
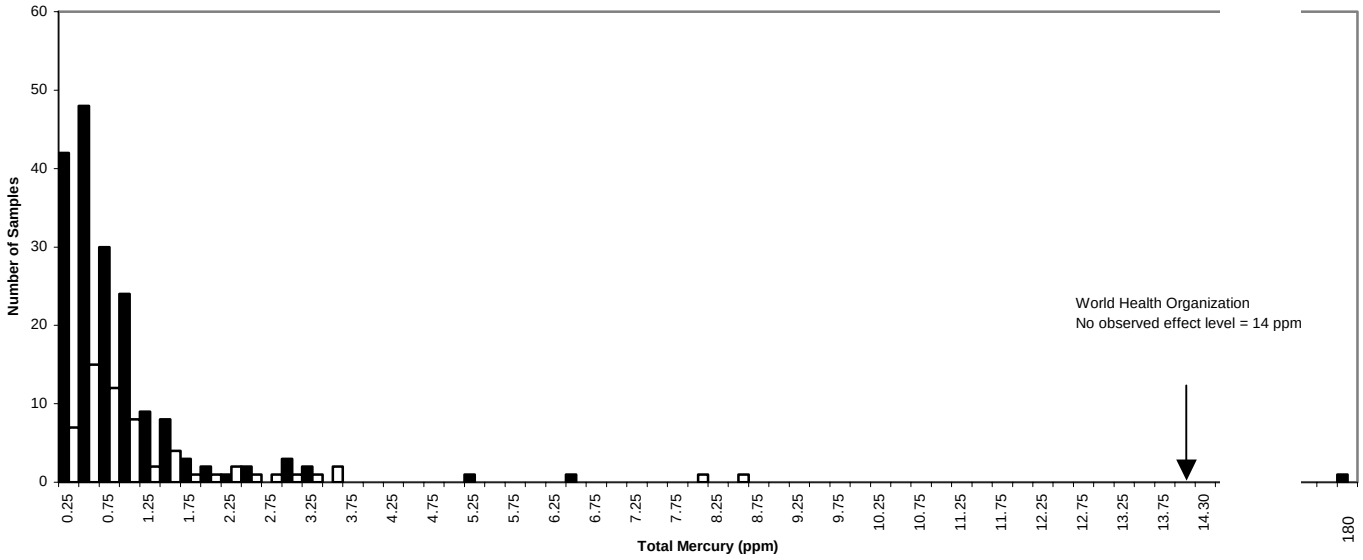


Figure 20. The Frequency Distribution of the Total Mercury Concentrations Detected in the Hair of Pregnant Women (n = 177; black bars; median = 0.47 ppm) Statewide and Nonpregnant Women of Childbearing Age (n = 60; white bars; median = 0.63 ppm) Participating in the Statewide Maternal Hair Mercury Biomonitoring Program.



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UNITS OF MEASURE

Milligram	**10^{-3}**	**one thousandth**	**0.001**
Microgram	**10^{-6}**	**one millionth**	**0.000001**
Nanogram	**10^{-9}**	**one billionth**	**0.000000001**
Picogram	**10^{-12}**	**one trillionth**	**0.000000000001**

parts per million = ppm = µg/g = mg/kg = ng/mg = mg/L

parts per billion = ppb = µg/kg = ng/g = µg/L

parts per trillion = ppt = pg/g = ng/kg = ng/L

0.01 mg/L = 10 µg/L

1 µmol mercury = 200 µg mercury = 1 µmol methylmercury