Technical Issue Paper

Health Benefits and Risks of Consuming Fish and Shellfish

DRAFT

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Table of Contents

Page

List of Figures and Tables ii
Figures ii
Tables ii

Acronyms & Abbreviations iii

Introduction 1

Analysis 2
I. Benefits associated with eating fish and shellfish 2
A. Seafood as a high quality protein source 2
B. Seafood as a source of essential fatty acids 2
C. Seafood as a source of nutrients (vitamins and minerals) 4
D. Seafood consumption and improved health outcomes 5
II. Risks associated with eating fish and shellfish 10
A. Brief summary of potential health effects 10
B. Adverse health effects associated with primary contaminants of concern 12
III. Comparison of health benefits and risks 15
A. Metrics for evaluating risks 15
B. Risk/Benefit Comparisons 15

Conclusions 26

References 27

List of Figures and Tables

Figures

Page

Figure 1. Decision pathway representing the balance between benefits and risks associated with seafood consumption (Source: Nesheim and Yaktine 2007).....23

Figure 2. EPA+DHA and mercury content in representative seafood portions. Source: Seafoodhealthfacts.org.....24

Tables

Page

Table 1. Frequency of consumption rank and concentrations of n-3 PFAs.....3

Table 2. Classification of the content of EPA plus DHA by total mercury content in 96 finfish and shellfish species 16

Table 3. Classification of the content of EPA + DHA by dioxin content in 76 finfish and shellfish species 17

Table 4. Estimated changes in child IQ resulting from maternal consumption of fish with different methylmercury and EPA plus DHA contents[a] 18

Table 5. Estimated changes in mortality per million people from consuming fish with different dioxin and EPA plus DHA contents [a] 19

Acronyms & Abbreviations

AD	Alzheimer's disease
AHA	American Heart Association
ALA	alpha-linoleic acid
AMD	age-related macular degeneration
BMD	bone mineral density
CHD	coronary heart disease
CKD	chronic kidney disease
CVD	cardiovascular disease
DDT	dichloro diphenyl trichloroethane
DEHP	di-ethylhexyl phthalate
DHA	docosahexaenoic acid
DPA	docosapentaenoic acid
Ecology	Washington State Department of Ecology
EPA	eicosapentaenoic acid
FAO	Food and Agriculture Organization of the United Nations
IOM	Institutes of Medicine
n-3 PFA or PUFA	Omega-3 polyunsaturated fatty acid
NSAID	nonsteroidal anti-inflammatory drug
PAH	polycyclic aromatic hydrocarbon
PBT	Persistent Bioaccumulative Toxics
PCB	polychlorinated biphenyl
PCDD	polychlorinated dibenzo-*p*-dioxin
PCDF	polychlorinated dibenzofuran
PTMI	provisional tolerable monthly intake
TCDD	2,3,7,8-tetrachlorodiobenzo-*p*-dioxin
TERA	Toxicology Excellence for Risk Assessment
TEQ	toxic equivalent
TSD	Fish Consumption Rates Technical Support Document
USDA	U.S. Department of Agriculture
USEPA	U.S. Environmental Protection Agency
WDOH	Washington Department of Health
WHO	World Health Organization

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Introduction

Multiple comments received by the Washington State Department of Ecology (Ecology) on the draft *Fish Consumption Rates Technical Support Document* (TSD) (Ecology 2011) asked why the TSD did not include a discussion of the relative benefits of consuming fish and shellfish or address the potential public health risks if people consume less fish. Others also suggested that the TSD should include some information regarding the contaminant concentrations in Washington State fish and shellfish.

Fish is a good source of protein and, unlike fatty meat products, it is not high in saturated fat. Fish is also a good source of omega-3 fatty acids. Omega-3 fatty acids benefit the heart of healthy people, and those at high risk of, or who have, cardiovascular disease. While some types of fish may contain high levels of mercury, PCBs (polychlorinated biphenyls), dioxins and other environmental contaminants, the American Heart Association recommends eating fish (particularly fatty fish) at least two times (two servings) per week.[1]

According to the Food and Agriculture Organization of the United Nations, worldwide fish consumption reached an all-time high in 2011, with an average consumption of 17 kg per person.[2]

This Technical Issue Paper summarizes the known health benefits of seafood consumption, the risks associated with a set of common contaminants in Washington State seafood, and compares these health benefits and risks.

Throughout this paper, use of the word "seafood" denotes fish and shellfish. A review of Washington State seafood contaminant concentrations and potential human exposures is presented in *Technical Issue Paper: Chemical Contaminants in Dietary Protein Sources.*

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[1] http://www.heart.org/HEARTORG/GettingHealthy/NutritionCenter/HealthyDietGoals/Fish-and-Omega-3-Fatty-Acids_UCM_303248_Article.jsp

[2] http://www.fao.org/news/story/en/item/50260/icode/

Analysis

I. Benefits associated with eating fish and shellfish

The most recent guidance from the American Heart Association (AHA) recommends eating fish, particularly fatty fish (e.g., salmon, anchovy, herring), at least two times per week (AHA 2012). The following sections describe why fish and shellfish are recommended as an important part of the diet.

A. Seafood as a high quality protein source

Fish is a good source of high quality protein that is not high in saturated fat (USDA 2010; AHA 2012). Saturated fats have a chemical makeup in which the carbon atoms are saturated with hydrogen atoms and are typically solid at room temperature. Eating foods that contain saturated fats raises the level of cholesterol in the blood. High levels of blood cholesterol increase the risk of heart disease and stroke. Many foods high in saturated fats are also high in cholesterol. Shellfish contain more cholesterol than most types of fish, but are very low in saturated fat (AHA 2012). A significant proportion of dietary fish intake is comprised of protein (Undeland et al. 2009). Fish proteins are considered easily digestible and are rich in essential amino acids (the building blocks of proteins) (review in Costa 2007). Essential amino acids are those that cannot be made by the body and must be supplied in the diet.

B. Seafood as a source of essential fatty acids

Omega-3 (n-3 polyunsaturated) fatty acids (n-3 PFAs) are essential fats that the body needs to function properly but cannot make on its own. Humans must get n-3 PFAs from foods. The n-3 PFAs that are particularly important in human nutrition include: alpha-linoleic acid (ALA), eicosapentaenoic acid (EPA), docosapentaenoic acid (DPA), and docosahexaenoic acid (DHA) (review in Mahaffey et al. 2011). EPA and DHA are important for human neurological development. These two n-3 PFAs play a role in: (1) cell membrane formation, integrity, and functions; (2) functioning of brain, retina, liver, kidney, adrenal glands, and gonads; and (3) local hormone production for the regulation of blood pressure and immune and inflammatory responses.

Humans can synthesize some of their requirement for long-chain PFAs from ALA (a short-chain PFA), but generally not in the amounts sufficient to meet dietary needs (review in Mahaffey et al. 2011). Fish is rich in the very long-chain n-3 PFAs EPA and DHA. Fish and shellfish acquire these PFAs by consuming algae (or other fish). Certain fatty fish (e.g., salmon, herring, sardines, mackerel) are also high in n-3 PFAs (Table 1). Some that are low in fat (e.g., trout and shrimp) are also good sources of n-3 PFAs.

Table 1. Frequency of consumption rank and concentrations of n-3 PFAs

Rank	Species	EPA + DHA (mg/100g fish)*
1	Shrimp	390
2	Tuna (all, average) Tuna canned – light (skipjack) Tuna canned – white (albacore) Tuna fresh – Bluefin (7 kg) Tuna fresh – Skipjack (3 kg) Tuna fresh – Yellowfin (5-20 kg)	630 128 – 270** 862 1,173 – 1,504** 256 – 328** 100 – 120**
3	Breaded fish products	0.26
4	Salmon	1,590
5	Crabs	36
6	Catfish	280
7	Other fish	54
8	Scallops	270
9	Lobster	360
10	Clams	240
11	Cod	240
12	Oysters	350
13	Other shellfish	310
14	Flatfish	15
15	Unknown fish	53
16	Pollock	260
17	Mussels	350
18	Trout	580
19	Haddock	180
20	Crayfish	380
21	Perch	300
22	Sardines	980
23	Swordfish	580
24	Bass (freshwater)	640
25	Sea bass	490
26	Pike	140
27	Mackerel – except King King mackerel	1,790 401
28	Shark	220
29	Walleye	530
30	Porgy	210

Source: Adapted from Mahaffey et al. 2011
*100 grams is equivalent to a 3.5-ounce serving
** range shown is raw vs. cooked

C. Seafood as a source of nutrients (vitamins and minerals)

Many Americans do not eat the variety and amounts of foods necessary to supply needed nutrients (USDA 2010). Seafood supplies a number of these essential vitamins and minerals, including: vitamins A, B3, B6, and B12, and D, and the minerals calcium, iron, selenium, and zinc (summarized from USEPA and TERA 1999; USDA 2010, others).

a. Vitamins

Vitamin A (retinol, retinal, retinoic acid) is a fat-soluble vitamin that is critical for vision, growth, bone development and maintenance, and immune function, among others. In general, fish is a better source of Vitamin A than beef, pork, or chicken, and higher-fat fish species contain more of this vitamin than lower-fat species. Some foods, such as milk, are fortified with this vitamin.

Vitamins B3 and B6 are water soluble – they must be supplied daily in the diet because the body stores these vitamins only briefly. Vitamin B3 (niacin, nicotinic acid, and nicotinamide) is involved in hydrogen transfer reactions and deficiency in the diet causes a condition called Pellagra, which is characterized by diarrhea, dermatitis, and dementia. Vitamin B6 exists as several different chemical structures that serve as important co-enzymes in various chemical reactions in the body that are involved predominantly in metabolism. Deficiency in Vitamin B6 is very rare in the United States. Vitamin B12 is important in normal functioning of the brain and nervous system and for the formation of blood. It is produced by microorganisms in animals and does not occur naturally in plant foods. Deficiencies of Vitamin B12 generally occur if absorption from food is impaired. Sport-caught fish (salmon, trout, channel catfish) are excellent sources of this vitamin.

Vitamin D is a fat-soluble vitamin that occurs naturally in several forms and can be synthesized in the skin when sun exposure is adequate. Vitamin D acts like a steroid hormone, controlling blood levels of calcium to affect bone, kidney, and intestinal tissues. Deficiency of Vitamin D leads to bone demineralization and a condition called osteomalcia (in children it is called rickets). Fish is among the best food sources of this vitamin. Some foods, such as milk and some packaged orange juices, are fortified with this vitamin.

b. Minerals

Calcium is necessary for bone health as well as nerve transmission, constriction and dilation of blood vessels, and muscle contraction. Low calcium intake is associated with low bone mass and risk of bone fractures. Dairy products provide about one-half of dietary calcium in the United States. Fish with soft bones (walleye, bass, and yellow perch), small fish eaten whole (sardines, smelts), and canned fish with bones (salmon) can contribute substantial amounts of calcium to the diet.

Iron is an essential part of many proteins and enzymes, including the proteins involved in oxygen transport (hemoglobin, myoglobin). It is also important in many enzyme oxidation/reduction reactions. Iron deficiency is the most common nutritional deficiency in the United States The heme form of iron, which is the most readily absorbed form, can be found in animal foods (meat fish). Seafood is a good source of heme iron.

Selenium, an essential nutrient, is present in the cells of all mammals. When bound to certain proteins, selenium acts as an antioxidant by detoxifying free radicals. Selenium must be supplied through dietary sources. Seafood and organ meats such as liver are the best sources of dietary selenium.

Zinc is part of many enzymes and deficiencies can cause stunted growth and delayed sexual maturation. In general, foods rich in protein are also good sources of zinc. Insufficient zinc levels are common in North America, particularly in vegetarians and adult women.

D. Seafood consumption and improved health outcomes

Seafood consumption is linked with improvements in health conditions including cardiovascular disease, arthritis, and cancer. The following sections summarize reviews of the published evidence regarding the various health benefits of seafood consumption. Where the evidence to support a link between seafood consumption and a specific health benefit is considered preliminary and further research is needed (e.g., with treatment of mood disorders), this is noted in the review for that condition.

There has been a tremendous amount of research into the health benefits of seafood consumption in recent years. A Google Scholar® search[3] of scientific literature using the keywords seafood +benefits +risk +review and limiting the results of the search to the last two years turned up over 2,700 articles and reports. McManus et al. (2010) provide a recent overview of health benefits from seafood consumption, although this is aimed toward benefits in the elderly. For this issue paper, the McManus et al. (2010) review was used as the basis for the discussion of health benefits and was augmented using primary literature and other reviews.

a. Cardiovascular disease/stroke

Over 81 million Americans (37 percent of the population) have cardiovascular disease (CVD) (AHA 2010). Major risk factors for CVD include high levels of blood cholesterol and other lipids, type 2 diabetes, hypertension (high blood pressure), metabolic syndrome, obesity, physical inactivity, and tobacco use. Hypertension affects 34 percent of Americans and is a major risk factor for heart disease, stroke, congestive heart failure, and kidney disease.

From McManus et al. 2010: “Strong evidence exists supporting the assertion that fish intake significantly contributes to the maintenance of heart health, protecting against cardio-vascular diseases, particularly ischemic stroke. Even a small amount of fish can provide a protective health effect for seniors. For example, 1 to 2 serves a week of oily fish (sardines, salmon, trout) is associated with a reduced rate of hospitalization and mortality, with the highest evidence for older women.”

Consumption of 1 to 2 fish meals per week lowers the relative risk of mortality from coronary heart disease (CHD) by 20 to 30 percent (Costa 2007). In fact, moderate evidence indicates that consumption of about 8 ounces of seafood per week is associated with reduced cardiac deaths among individuals with and without pre-existing CVD (AHA 2010). DHA and EPA in the diet likely reduce the risk of fatal CHD by reducing cardiac arrhythmias (Harris et al. 2009). An

[3] http://scholar.google.com/

arrhythmia is a problem with the rate or rhythm of the heartbeat – too slow, too fast, or with an irregular rhythm. A review by Dórea (2008) found two studies indicating that the cardiovascular benefits of fish are due not only to the n-3 PFAs but also to the fish proteins. Even short-term DHA + EPA consumption (> 1 to 2 g/day) favorably affects many physiological measures of cardiovascular risk including blood pressure, resting heart rate, triglyceride levels, and possibly heart rate variability (Harris et al. 2009). Other reviews have concluded that n-3 PFAs alone do not have a clear effect on total mortality or combined CVD events and that positive effects were only seen when taking into account fish-based studies (Undeland et al. 2009). This suggests that other, non-n-3 PFA compounds in fish contribute to cardio-protective and neuro-protective value of fish consumption. For example, Vitamin D insufficiency has been related to CVD, and reduced Vitamin D status has been associated with several CVD risk factors including blood pressure and body-mass index.

Evidence for effects on stroke is mixed. Meta-analyses indicate a 30 percent lower risk of ischemic stroke with fish intake of ≥ 1 meal/week compared with < 1 meal/month (Harris et al. 2009). Ischemic stroke involves blockage of the arteries leading to the brain caused by artherosclerosis and thrombosis (Undeland et al. 2009). The mechanisms protecting against ischemic stroke are believed to be the same as those for CHD.

b. Arthritis

McManus et al. (2010) state that "the risk of developing arthritis is reduced in adults by regularly consuming around 3500-4000 mg of marine source (oily fish) omega-3 PUFAs each week. Furthermore, ingestion of oily fish can reduce inflammation and joint tenderness associated with all forms of inflammatory arthritis. Fish oil is currently used as an adjuvant to approved medications for arthritis and studies support its efficacy in conjunction with nonsteroidal anti-inflammatory drugs (NSAIDs). While consumption of fish and fish oil does not prove efficacious in all cases, some individuals have been able to 'discontinue or reduce NSAID therapy' while continuing fish oil ingestion."

Greater intake of Vitamin D is also associated with lower risk for rheumatoid arthritis and improvement in rheumatoid arthritis patients (Undeland et al 2009). Vitamin D could have an immunosuppressive role in these effects, but more research is needed (Undeland et al. 2009).

c. Cancer

McManus et al. (2010) state that "high fish intake has been associated with significantly reduced risk of ovarian and colorectal cancer. Furthermore, findings from a recent United Kingdom Women's Cohort Study of 35,372 women supports the assertion that postmenopausal women who consumed fish experienced a significantly reduced risk of breast cancer when compared with red meat consumers, indicating reduced risk in older women who prefer fish as a primary protein source to the exclusion of red meat. High level evidence supports fish consumption as protective in reducing the risk of prostate and lung cancers in males. Increased consumption of seafood also confers protection against the development of esophageal cancer in males aged 45 years and older in large population-based studies."

Undeland et al. (2009), summarizing the benefits of seafood consumption, stated that observational studies[4] on fish consumption have shown protection for risk of digestion tract cancers (oral cavity and pharynx, esophagus, stomach, colon, and rectum) and also for ovary, pancreas, larynx, and endometrial cancers. Prospective[5] and case-control[6] studies, however, either do not show an association between fish intake and cancer risk, or only show reduced risk at high fish intake levels. Harris et al. (2009) states that the preponderance of evidence for anticarcinogenic effects of EPA + DHA is weak despite persuasive data from animal models and cultured tumor cell lines. However, a review and meta-analysis of fish consumption and prostate cancer risk that found no strong evidence of a protective association between fish consumption and prostate cancer risk did show a significant 63 percent reduction in prostate cancer-specific mortality (Scymanski et al. 2010).

d. Macular degeneration

Many studies support the significant protective effects of a diet high in seafood. Age-related macular degeneration (AMD) is a deterioration or breakdown of the eye's macula and is a common eye condition among people age 50 and older. The macula is the part of the eye that provides sharp, central vision needed for seeing objects clearly. AMD is a leading cause of vision loss in older adults. According to McManus et al. (2010), "it is becoming increasingly apparent as further scientific research emerges that regular fish and seafood consumption may reduce the likelihood of age-related macular degeneration (AMD) with the odds of AMD '51% lower in the highest quartile of fish intake compared to the lowest quartile'."

Recently, a cohort study of female medical professionals (over 38,000 with average age of 54) found regular consumption of DHA and EPA and fish was associated with significantly decreased risk of incident AMD and may be of benefit in primary prevention of AMD (Christen et al. 2011). Women who consumed one or more servings of fish per week, compared with those who consumed less than one serving per month, had a relative risk of AMD of 0.58.

e. Cognitive function

According to McManus et al. (2010), "omega-3 PUFAs in seafood play an important role in neurological structure and function. Docosahexaenoic acid (DHA), a long-chain marine PUFA found in seafood, is a catalyst for the slowing of early stage progression of dementia. Further study is expected to shed light on how DHA potentially prevents the neurological damage that results from dementia." The review further states that "research from marine and human epidemiological studies suggest that 'higher fish consumption is associated with better cognitive function in later life', enabling resistance to cognitive decline. Recent evidence strongly associates a dietary profile in which fish features prominently, with lower risk of developing Alzheimer's disease (AD) and maintaining cognitive function. Evidence increasingly supports the assertion that marine source omega-3 PUFAs in fish play a role in delaying onset and

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[4] An observational study draws inferences about the possible effect of a treatment on subjects, where the assignment of subjects into a treated group versus a control group is outside the control of the investigator.

[5] An analytical study designed to determine the relationship between a condition and a characteristic shared by some members of a group.

[6] An analytical study which compares individuals who have a specific disease ("cases") with a group of individuals without the disease ("controls").

arresting the progression of AD, though further studies are needed to investigate the mechanism involved."

The EHA and DHA review by Harris et al. (2009) found that the available evidence for protective effects of long-chain PUFAs from fish on the risk of dementia is promising but limited. Epidemiological evidence is positive for benefits of just one fish meal per week on the risk of Alzheimer's disease, dementia, and cognitive decline. Animal evidence supports a protective relationship of n-3 PFAs on neurodegeneration of the brain with aging, and several studies in progress in the United States and Europe should shed more light on this relationship.

f. Hearing loss

McManus et al. (2010) state that "recent research suggests that marine source omega-3 PUFAs may have a protective effect in preventing or delaying age-related hearing loss (presbycusis). Consumption of at least two servings of fish per week significantly reduced the risk of presbycusis in a recent study…" Gopinath et al. (2010) found an inverse association between higher intakes of long-chain n-3 PFAs and regular weekly consumption of fish and hearing loss. Higher dietary intake of long-chain n-3 PFAs was associated with a 24 percent decreased risk of developing incident hearing loss. Regular consumption of fish in the diet was negatively associated with the 5-year incidence and progression of hearing loss in older adults. These data suggest that n−3 fatty acids and fish have a role in maintaining healthy auditory function.

g. Depression/mood

According to McManus et al. (2010), "intake of omega-3 PUFA rich seafood is linked to increased dispositional optimism in the elderly, and has, in some long term studies, been linked to reduced depression, with a recent meta-analytic review of polyunsaturated fatty acid levels in patients with depression concluding that 'n-3 polyunsaturated fatty acids play a role in the pathogenesis of depression'. Therefore, omega-3 PUFA rich seafood could benefit individuals suffering from depression. Further research on the possible role of seafood consumption in moderating depression is required for these findings to be substantiated."

Hegarty and Parker (2011) reviewed the evidence implicating marine n-3 PFAs in the etiology [causes or origin] of depressive and bipolar disorders and the effect of n-3 PFA supplementation in the treatment of those disorders. The authors focused primarily on studies conducted within the previous 5 years, and found the following: (1) the evidence suggests a contributory etiological role of n-3 PFA deficiency to depressive and bipolar disorders; (2) a growing body of evidence implicates inflammatory processes in the etiology and/or progression of depression; (3) n-3 PFAs play a role in modulating the n-6 PFA derived pro-inflammatory molecules and are able to suppress the expression of a wide variety of inflammatory genes; (4) a recent meta-analysis concluded that levels of EPA, DHA, and total n-3 PFAs are significantly lower in depressed patients compared to controls; (5) trials of EPA-rich n-3 PFA supplements were more effective in treating depressive symptoms than DHA-rich preparations; and (6) an increasing number of trials do not support n-3 PFA supplementation as an effective treatment for major depressive disorder or postnatal depression. Hagarty and Parker (2011) concluded that more research focusing on EPA-rich supplements is warranted and that, even with many questions remaining, two fish servings per week would be recommended with supplementation for those with depressive or bipolar disorders. They believe it is possible that n-3 PFA supplementation

may be of benefit for mood disorders but that research has not yet established the right dose and/or the right constituent ratio.

h. Osteoporosis

McManus et al. (2010) state that "seafood is a rich source of both calcium and Vitamin D, important bone-building micronutrients. Vitamin D rich seafood can play an important role in the maintenance of bone mineral density as people age. Potential reduced sun exposure and an increased requirement of Vitamin D in older people underpins the need for high quality, bioavailable Vitamin D. Seniors also have a reduced capacity to 'synthesize provitamin D3 in skin and to hydroxylate vitamin D3 in kidneys. It is widely recognized that a diet high in oily fish prevents vitamin D deficiency; and commonly consumed, affordable sources of seafood such as Australian salmon and silver perch contain more than double the recommended daily intake of Vitamin D in a 150 g serve. A 150 g serve of Australian Salmon will also deliver more than half the recommended daily intake of calcium. Calcium requirements increase with age and seafood presents rich serves of calcium combined with optimal amounts of Vitamin D to aid its absorption, protecting bone mineral density (BMD).

Loss of calcium through urinary excretion is of concern to bone health. Evidence is emerging showing lower fractures and higher bone mineral density with the consumption of adequate levels of calcium rich, high protein seafood. This may be due to increased intestinal absorption, which negates the impact of urinary excretion. When calcium and vitamin D intake is adequate, dietary protein at moderate levels is beneficial to total body BMD particularly for seniors. Seafood is a good source of calcium, vitamin D, and protein [and] therefore can favorably contribute to BMD.

High intake of sea fish is independently associated with greater bone mass and lower osteoporosis risk in women, especially those consuming more than 250 grams per week of seafood."

i. Recent Research

The following summaries do not represent the results of an exhaustive literature search, which is outside the scope of this review, but are articles of interest that were found when searching for recent reviews on the benefits of seafood consumption. These articles are too new to have made it into the review papers that were published recently.

Gopinath et al. (2011) investigated the association between dietary intakes of PFA (n-3, n-6 and α-linoleic acid), fish and the prevalence of chronic kidney disease (CKD). Due to the anti-inflammatory properties of PFA, it has been suggested that they may protect against kidney damage in adults. These researchers found that an increased dietary intake of long-chain n-3 PFA and fish reduced the prevalence of CKD. Therefore, a diet rich in n-3 PFA and fish could have a role in maintaining healthy kidney function.

In a case-control study of maternal dietary patterns and congenital heart defects, a dietary pattern characterized by the high intake of fish and seafood was associated with a reduced risk of congenital heart defects in offspring (Obermann-Borst et al. 2011). Based on these findings, the researchers suggested further investigation in a randomized intervention trial was warranted.

Changing human dietary patterns in the last 100–150 years have given rise to an imbalance in the dietary ratio of n-6 and n-3 PFAs (review in Candela et al. 2011). This ratio used to be around 1–2:1 but in Western diets is now as high as 20–30:1. n-3 PFA intake is much lower today due to factors such as decreased fish consumption while n-6 PFA intake is higher due to factors such as increases in n-6 rich grains and vegetable oils. Although n-6 and n-3 PFAs exert opposing effects on inflammatory activity (n-3 PFAs reduce inflammation), high n-6:n-3 ratios have not been correlated with high inflammatory marker levels. Some researchers point to the need to decrease n-3 PFA intakes while others call for increasing n-3 PFA intakes to mediate the imbalance in the ratio. Beneficial effects on asthma (an inflammatory disease) have been seen at ratios of 5:1 with adverse effects seen at ratios of 10:1 (review in Candela et al. 2011). With regard to cancers, a high n-6:n-3 ratio was associated with increased prostate cancer risk in a recent study (Williams et al. 2011).

II. Risks associated with eating fish and shellfish

Risks associated with eating fish and shellfish include the risk from chemical contaminants (fish and shellfish) and pathogens or biotoxins (generally in shellfish).

According to the U.S. Environmental Protection Agency (USEPA) 2010 listing of fish consumption advisories (USEPA 2011), all 50 states have fish consumption advisories in place to protect their residents from the potential health risks of eating contaminated fish caught in local waters. As of 2010, 42 percent of the nation's total lake acreage and 36 percent of the nation's total river miles were under advisories. There were consumption advisories for 33 different environmental pollutants in the United States in 2010—a total of 4,598 fish consumption advisories were in effect. Three pollutants—methylmercury, PCBs, and dioxins—were responsible for nearly 90 percent of the advisories. These contaminants accumulate in fish tissue at concentrations many times higher than concentrations in the water and can persist for years in sediments.

Some shellfish species feed by taking in large volumes of water and filtering out the food particles (WDOH 2012). These filter-feeding species, such as oysters, clams, and mussels, can accumulate natural biotoxins as well as pathogens (e.g., norovirus, fecal coliforms, and vibrio) in their edible tissues. The Washington Department of Health (WDOH) Shellfish Program monitors for biotoxins such as paralytic shellfish poison and domoic acid in shellfish and closes harvest areas when levels pose a threat to public health. The Shellfish Program also classifies shellfish growing areas, monitors marine water for pollution, licenses and inspects commercial growers, and provides recreational harvesters with information about where, when, and what type of shellfish are safe to harvest. Washington State shellfish consumers can minimize their risks of becoming ill from shellfish biotoxins and pathogens by avoiding raw shellfish (proper cooking kills pathogens although it does not neutralize biotoxins) and complying with shellfish harvesting restrictions when the Shellfish Program closes harvest areas. This issue paper focuses on chemical contaminants in seafood and so pathogens and biotoxins are not discussed further.

A. Brief summary of potential health effects

Toxic contaminants enter Washington's ecosystems via water (e.g., river or stream inputs, industrial discharges, stormwater runoff), the atmosphere, and in the bodies of migrating

organisms. Some chemicals in the environment pose an immediate health threat. Others gradually build up in the environment and, in humans, can cause disease long after exposure. Contaminants in sediment and water may accumulate in fish and shellfish through processes called bioaccumulation and bioconcentration. Bioaccumulation is the accumulation of chemicals in the tissue of fish or shellfish through respiration, ingestion, or direct contact with contaminated water, sediment, and pore water in the sediment. Bioconcentration is the process of accumulation of water-borne chemicals by fish or shellfish through non-dietary routes. Some contaminants are biomagnified up the food chain. This occurs when the tissue concentration increases at each trophic level in the food chain when there is efficient uptake of the contaminant but slow elimination. Hydrophobic chemicals—those that adhere to organic particles in sediments—tend to be bioaccumulative. Two types of contaminants that may occur in seafood are metals and organics. These are described below.

a. Metals

Metals include essential trace elements required for human health, such as zinc and copper, and those without any known human dietary need, such as lead and mercury. Many metals, even those considered essential in the diet, can be toxic at high enough doses. Some metals are widespread in the environment due to natural processes (e.g., arsenic) but have increased locally or globally due to human activities (Eisler 2000). Metals contamination occurs throughout the state from a variety of sources such as industrial releases, deterioration or wear of roofing and other materials, batteries, paints, and dyes. Methylmercury, an organic form of mercury, is included in a class of contaminants termed Persistent Bioaccumulative Toxics (PBTs).[7] PBTs are of concern because they resist degradation, bioconcentrate from the environment (e.g., water, sediments) into organisms, and may biomagnify up food chains (PSAT 2007).

b. Organics

Organic contaminants are natural or manmade chemicals that include several PBTs: dioxin and dioxin-like compounds (polychlorinated-dibenzo-p-dioxins [PCDDs], polychlorinated-dibenzo-furans [PCDFs], and polychlorinated biphenyls [PCBs]), polycyclic aromatic hydrocarbons (PAHs), and organochlorine pesticides (e.g., chlordane, DDT).

PAHs are a group of organic chemicals that have a fused ring structure of two or more benzene rings, and are formed during the incomplete combustion of organic materials. PAHs are ubiquitous in nature, largely as the result of natural processes such as forest fires and microbial synthesis. Anthropogenic sources of PAHs include vehicle exhaust; manufacturing of coal tar pitch and asphalt; petroleum refining; and open burning (Eisler 2000 and others). The largest sources of PAHs in Washington are wood burning stoves and fireplaces. Other major sources include creosote-treated wood, vehicles, leaks and improper disposal of motor oil, and small engines (e.g., lawn mowers and garden equipment). PAHs in fish and shellfish are a result of contamination of water and sediment while PAHs in livestock (e.g., beef) are from consumption of contaminated pasture and vegetation. PAHs may accumulate in shellfish but generally do not

[7] Two metals (cadmium and lead) are considered PBT metals of concern in Washington State (Washington Administrative Code 173-333) but these metals are not always analyzed in seafood tissue samples and do not often appear in articles and reports regarding PBTs in seafood in Washington.

biomagnify because most are readily metabolized by other species such as fish and humans (Eisler 2000).

Dioxin-like compounds include PCDDs, PCDFs, and certain PCBs. PCDDs and PCDFs have natural sources but are also created and are considered unwanted impurities in some industrial processes and products such as pesticides (Eisler 2000). Common sources of dioxins in Washington State include waste incinerators, pulp mills, industrial processes, and backyard burn barrels. PCBs are a group of 209 synthetic organic chemicals that were used as insulating and cooling agents in the electricity generating industry, and that had a number of other industrial applications (e.g., as additives to caulks and paints to improve durability). The production and sale of PCBs was banned in the United States in the late 1970s, but these compounds have persisted in the environment in soils, sediments, and organisms. Dioxins and PCBs bioaccumulate and biomagnify in the food chain.

c. Primary chemicals of concern in Washington fish and shellfish

Fish and shellfish in Washington State have been exposed to pollutants discharged into waters including sewage, pulp and paper industry wastes, petroleum products, heavy metals, and synthetic organic chemicals (e.g., pesticides, PCBs). Accidental spills of dangerous materials and past business practices have contaminated land and waters. In 2006, WDOH reviewed Puget Sound fish tissue data from the Washington Department of Fish and Wildlife to determine which contaminants have the potential to cause public health concern (WDOH 2006). The following chemicals were detected in 10 percent or more of the samples: alpha chlordane, arsenic, benzyl alcohol, copper, DDT and degradation products, DEHP, mercury, and PCBs. Of these chemicals, only PCBs and mercury were detected with sufficient frequency and at high enough levels that WDOH believed an assessment of health risk was warranted at that time. WDOH did not include shellfish in the risk assessment. Some shellfish are known to accumulate PAHs due to their inability to metabolize these compounds. Therefore, because shellfish may be a significant source of PAHs for shellfish consumers, PAHs were included in this Technical Issue Paper. Note that the Puget Sound Assessment and Monitoring Program did not analyze tissues for PCDDs or PCDFs. However, data from the fish and shellfish studies in the Ecology Environmental Information Management Database indicate that these chemicals are found in Washington State fish and shellfish. This Technical Issue Paper focuses on the health risks associated with mercury, PAHs, dioxins/furans, and PCBs.

B. Adverse health effects associated with primary contaminants of concern

a. Mercury

Mercury and mercury compounds have no known biological function and their presence in biological organisms is undesirable and potentially hazardous (review in Eisler 2000). Most atmospheric mercury is in elemental or inorganic forms while the mercury in water, soil, plants, and animals is generally in organic forms. Bacteria in the environment convert inorganic mercury to organic forms such as methylmercury. Methylmercury is considered the most hazardous mercury compound due to its high stability, its lipid solubility, and its ability to penetrate

membranes in living organisms. Methylmercury can bioconcentrate in organisms and biomagnify up food chains. Organic mercury can cross the blood-brain barrier[8] and the placenta. For all organisms tested, early developmental stages were the most sensitive to mercury poisoning, and organic forms were more toxic than inorganic forms. Mercury is not concentrated in fat but is associated with protein and therefore in animal-based foods it is found in the meat/fillet.

Mercury is a known teratogen (causing birth defects), mutagen (causing DNA mutations), and carcinogen (review in Eisler 2000). Mercury can adversely affect reproduction, growth and development, behavior, blood serum chemistry, motor coordination, vision, hearing, histology, and metabolism at low concentrations.

b. Arsenic

Arsenic is bioconcentrated but does not biomagnify in food chains (Eisler 2000). Therefore, arsenic concentrations are usually low in most organisms. Exposure to inorganic arsenic is generally from contaminated drinking water (WDOH 2009). Arsenic in food sources including seafood is generally in organic forms, primarily arsenobetaine. Arsenobetaine is very stable; after ingestion, it is rapidly excreted unchanged in the urine (summary in Vahter 1994).

Acute or subacute exposure to arsenic compounds can cause appetite loss, reduced growth, hearing loss, dermatitis, blindness, degenerative changes in the kidney and liver, cancer, chromosomal damage, birth defects, and death (review in Eisler 2000). Chronic exposure to arsenic compounds is associated with liver, kidney, and heart damage, hearing loss, brain-wave abnormalities, and impaired resistance to viral infection. However, the probability of chronic poisoning from continuous ingestion of small doses is rare due to the body's ability to detoxify and excrete arsenic rapidly.

In mammals, inorganic arsenic compounds are more toxic than organic arsenic compounds, and trivalent species (As^{+3}) are more toxic than pentavalent (As^{+5}) species (review in Eisler 2000). Ingestion of inorganic arsenic increases the risk of cancer of the skin, lungs, bladder, and kidneys. Early developmental stages are the most sensitive to arsenic. Inorganic arsenic can cross the placenta and produce mutagenic, teratogenic, and carcinogenic effects in offspring. However, at environmentally relevant levels and routes of exposure, humans are not at risk of birth defects from arsenic.

c. PAHs

Exposure to PAHs may occur through the lungs, stomach, or skin. Of these pathways, dietary intake is a major source of exposure for PAHs (Diggs et al. 2011). Chronic exposure can cause dermatitis and hyperkeratosis. Benzo(a)pyrene is considered to be one of the most toxic PAH compounds and is the PAH with the most available health effects data. The USEPA classifies benzo[a]pyrene as a probable human carcinogen based on multiple studies with rats and mice. According to a Joint Food and Agriculture Organization of the United Nations (FAO) / World Health Organization (WHO) Expert Committee report (WHO 2006), 13 PAHs are clearly carcinogenic and 15 PAHs are

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[8] The blood-brain barrier is a semi-permeable membrane that allows some materials to cross but prevents others from crossing; it protects the brain from foreign substances, protects the brain from hormones and neurotransmitters from other parts of the body, and maintains a constant environment for the brain.

genotoxic in experimental animals. Cancer associated with exposures to PAH containing mixtures occurs mainly in the lung (inhalational exposure) and skin (dermal exposure). Ingestion of PAHs has been associated with esophageal cancer (Diggs et al. 2011).

d. PCDD/Fs

Dioxin-like compounds (referred to hereafter as dioxins) include PCDDs, PCDFs, and PCBs. Dioxins and furans are discussed here, while PCBs are discussed below. Dioxins affect the immune system and cause dermal and hepatic (liver) toxicity, a variety of endocrine (hormone) effects, and cancer (summary in Birnbaum and Fenton 2003; others). The embryo and fetal stage of development may be especially susceptible to dioxin effects (Birnbaum 2005). Dioxins are tumor promoters that cause tumors to grow and enhance the incidence and multiplicity of tumors at multiple sites in the body. Dioxins are persistent, accumulating and lasting in the body for years. For maternal to offspring exposure to dioxins (e.g., through placenta and breast milk), the majority, if not all, of the effects are associated with *in utero* exposure (Birnbaum 2005). Nursing leads to greater infantile exposure through the breast milk, but this does not have long-term effects on the adult body burden.

The mechanism of action for dioxin effects on vertebrate species is through activation of the aryl hydrocarbon receptor (Ah-receptor) (White and Birnbaum 2009). The Ah-receptor is believed to play key roles in development, aging, hypoxia, and circadian rhythms. Laboratory test animals that are missing the Ah-receptor[9] are not healthy, which highlights that the receptor and its controlled activation are necessary for well-being (summary in Tuomisto and Tuomisto 2012).

Experiments with animals have shown dioxin to be a multi-site carcinogen, but there is limited evidence for the carcinogenicity of dioxin in humans at environmentally relevant concentrations, and this issue is extremely controversial. Epidemiological studies of dioxin exposures and effects are complicated by the fact that everyone has some exposure to dioxins and to other chemicals, and carry body burdens of a suite of chemicals. Recently, Boffetta et al. (2011) conducted a critical review of the epidemiologic studies on human exposures to 2,3,7,8-tetrachlorodiobenzo-*p*-dioxin (TCDD) and cancer and concluded that "recent epidemiological evidence falls far short of conclusively demonstrating a causal link between TCDD exposure and cancer risk in humans." This finding is mirrored in the review by Tuomisto and Tuomisto (2012) who concluded that "Occupational cohorts with the highest exposures imply that there is a small risk of all cancers combined, but it is difficult to pinpoint the confounding effect of the main chemicals. Studies after major accidents do not unequivocally confirm this risk. The risks to populations *at the current dioxin levels*[10] seem trivial if present at all."

e. PCBs

Similar to dioxins, PCBs are lipophilic and move through the placenta and into milk (review in Santerre 2008). The USEPA has classified PCBs as a probable human carcinogen (USEPA 2012). Only a few PCBs are structurally similar to dioxin and therefore are considered to be dioxin-like in their toxic effects (i.e., toxicity mediated by induction of the Ah-receptor). The non-cancer effects of PCBs may include: immune system suppression, reproductive effects such

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[9] Animals that are bred specifically without the receptor to study drug toxicity and the biological function of the receptor.

[10] Emphasis added.

as reduced birth weight, neurological effects such as learning deficits and changes in activity, and endocrine effects such as changes in thyroid hormone levels (USEPA 2012). The different health effects of PCBs may be interrelated, as alterations in one system may have significant implications for the other regulatory systems of the body. PCBs and dioxins are rarely found in environmental and biological samples in the absence of one another (White and Birnbaum 2009).

III. Comparison of health benefits and risks

This section describes the metrics used in evaluating the risks associated with contaminants and presents comparisons of health benefits to risks of seafood consumption. The risk assessments are presented by date order, with the most recent described first.

A. Metrics for evaluating risks

Contaminants can cause a variety of health effects including cancer and non-cancer health effects. The metrics used to evaluate risks from contaminants differ depending on if the toxic endpoint is cancer or not cancer (e.g., neurotoxicity, immunotoxicity). The following paragraphs, modified from USEPA and TERA (1999), describe the most commonly used metrics for these two types of endpoints.

Cancer slope factors are estimates of risk that are derived from dose-response data from laboratory animal or human epidemiology studies. Traditionally, a linearized multi-stage model has been used to extrapolate from what is observed at high experimental concentrations to lower environmental exposure levels. This cancer potency is estimated as the 95 percent upper confidence limit of the slope of the dose-response curve in the low dose region. This is an upper estimate of risk and the actual risk may be much lower or even approach zero. USEPA proposed revised cancer guidelines in 1996 and additional proposed guidance in 1998, which recommend that the mode of action be considered. The guidance recommends that a linear extrapolation should be used if the chemical is believed to act via a genotoxic mode of action, if the mode of action is expected to be linear at low doses, or (as a default) if no mode of action data are available. The guidance also recommends that a non-linear approach to extrapolation to low doses should be used when sufficient information on mode of action warrants.

For non-cancer endpoints, a reference dose is identified at which one would not expect to see adverse effects in a population (including sensitive subgroups). A single estimate of a “safe” dose is identified from animal or human data, using the No Observed Adverse Effect Level (NOAEL). This is divided by uncertainty factors to account for extrapolation from animals to humans, variability in the human population, and deficiencies in the database of studies on the substance. The resulting reference dose (RfD) is defined as “an estimate (with uncertainty perhaps spanning an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime.”

B. Risk/Benefit Comparisons

a. FAO/WHO (2011)

In January 2010, the FAO and WHO convened a Joint Expert Consultation on the Risks and Benefits of Fish Consumption (FAO/WHO 2011). The tasks of the Expert Consultation were to

review data on levels of nutrients (long-chain n-3 PFAs) and two chemical contaminants (methylmercury and dioxins) in a range of fish species and to compare the health benefits of fish consumption and nutrient intake with the health risks associated with contaminants present in fish.

After reviewing the literature, the Expert Consultation decided to compare the effects of (1) prenatal exposure to long-chain n-3 PFAs (EPA and DHA) and methylmercury on child IQ and (2) exposure to long-chain n-3 PFAs and dioxins on mortality. The rationale for this choice was based on the common health end-points and relatively robust evidence to establish dose–response relationships from multiple cohort studies.

Using data on over 75 species of fish and shellfish, the Expert Consultation classified the content of n-3 PFAs (as EPA + DHA) by total mercury content and by dioxin content (as total TEQs) (Tables 2 and 3). The resulting matrices were produced using those classifications:

Table 2. Classification of the content of EPA plus DHA by total mercury content in 96 finfish and shellfish species

		EPA + DHA			
		x ≤ 3 mg/g	3 < x ≤ 8 mg/g	8 < x ≤ 15 mg/g	x > 15 mg/g
Mercury	x ≤ 0.1 µg/g	Fish: butterfish; catfish; cod, Atlantic; cod, Pacific; croaker, Atlantic; haddock; pike; plaice, European; pollock; saithe; sole; tilapia Shellfish: clams; cockle; crawfish; cuttlefish; oysters; periwinkle; scallops; scampi; sea urchin; whelk	Fish: flatfish; John Dory; perch, ocean and mullet; sweetfish; wolf fish Shellfish: mussels; squid	Fish: redfish; salmon, Atlantic (wild); salmon, Pacific (wild); smelt Shellfish: crab, spider; swimcrab	Fish: anchovy; herring; mackerel; rainbow trout; salmon, Atlantic (farmed); sardines; sprat Fish liver: cod, Atlantic (liver); saithe (liver) Shellfish: crab (brown meat)
	0.1 < x ≤ 0.5 µg/g	Fish: anglerfish; catshark; dab; grenadier; grouper; gurnard; hake; ling; lingcod and scorpionfish; Nile perch; pout; skate/ray; snapper, porgy and sheepshead; tuna, yellowfin; tusk; whiting Shellfish: lobster; lobster, American	Fish: bass, freshwater; carp; perch, freshwater; scorpion fish; tuna; tuna, albacore Shellfish: crab; lobster, Norway; lobsters, spiny	Fish: bass, saltwater; bluefish; goatfish; halibut, Atlantic (farmed); halibut, Greenland; mackerel, horse; mackerel, Spanish; seabass; seabream; tilefish, Atlantic; tuna, skipjack	Fish: eel; mackerel, Pacific; sablefish
	0.5 < x ≤ 1 µg/g	Fish: marlin; orange roughy; tuna, bigeye	Fish: mackerel, king; shark	Fish: alfonsino	Fish: tuna, Pacific bluefin
	x > 1 µg/g		Fish: swordfish		

Table 3. Classification of the content of EPA + DHA by dioxin content in 76 finfish and shellfish species

		EPA + DHA			
		x ≤ 3 mg/g	3 < x ≤ 8 mg/g	8 < x ≤ 15 mg/g	x > 15 mg/g
Dioxins	x ≤ 0.5 pg TEQ/g	Fish: anglerfish; catshark; cod, Atlantic; grenadier; haddock; hake; ling; marlin; orange roughy; pollock; pout; saithe; skate/ray; sole; tilapia; tuna, bigeye; tuna, yellowfin; tusk; whiting Shellfish: cockle; clams; crawfish; cuttlefish; periwinkle; scallops; scampi; sea urchin	Fish: flatfish; John Dory; perch, ocean and mullet; shark; sweetfish; tuna, albacore	Fish: redfish; salmon, Pacific (wild); tuna, skipjack	
	0.5 < x ≤ 4 pg TEQ/g	Fish: catfish; dab; gurnard; plaice, European Shellfish: lobster; oysters; scallops; whelk	Fish: scorpion fish; swordfish; tuna Shellfish: mussels; squid	Fish: alfonsino; goatfish; halibut, Atlantic (farmed); halibut, Greenland; mackerel, horse; salmon, Atlantic (wild); seabass; seabream	Fish: anchovy; herring; mackerel; mackerel, Pacific; rainbow trout (farmed); salmon, Atlantic (farmed); tuna, Pacific bluefin Shellfish: crab (brown meat)
	4 < x ≤ 8 pg TEQ/g			Shellfish: crab, spider	Fish: sardines; sprat
	x > 8 pg TEQ/g			Fish: bluefish	Fish: eel Fish liver: cod, Atlantic (liver); saithe (liver)

For the risk-benefit comparisons, the Expert Consultation created matrices for the calculations of (1) the effects on child IQ as a result of the mother consuming one, two, four, or seven servings of fish per week with different n-3 PFA and methylmercury concentrations (Table 4), and (2) the effects on mortality as a result of consuming one, two, four, or seven servings of fish per week with different n-3 PFA and dioxin concentrations (Table 5). The matrices for the effects of methylmercury show estimates of IQ lost as a result of methylmercury exposure in red and estimates of IQ points gained as a result of n-3 PFA exposure in green. Shaded cells represent estimates of where the net effect on child IQ (using the upper-bound estimate) is negative. The matrices for the effects of dioxins show estimates of lives lost as a result of dioxin exposure in red and estimates of lives saved (due to reduction in coronary heart disease) as a result of n-3 PFA exposure in green. Shaded cells represent estimates of where the net effect is negative—lives lost are greater than lives saved.

Table 4. Estimated changes in child IQ resulting from maternal consumption of fish with different methylmercury and EPA plus DHA contents[a]

(a) One serving per week (3.5 ounces per week, or 14.3 g/day)

			EPA + DHA			
			x ≤ 3 mg/g	3 < x ≤ 8 mg/g	8 < x ≤ 15 mg/g	x > 15 mg/g
		Median	2	5.5	11.5	20
Methylmercury	x ≤ 0.1 µg/g	0.05	–0.02, –0.08 +0.77	–0.02, –0.08 +2.1	–0.02, –0.08 +4.4	–0.02, –0.08 +5.8
	0.1 < x ≤ 0.5 µg/g	0.3	–0.12, –0.47 +0.77	–0.12, –0.47 +2.1	–0.12, –0.47 +4.4	–0.12, –0.47 +5.8
	0.5 < x ≤ 1 µg/g	0.75	–0.30, –1.2 +0.77	–0.30, –1.2 +2.1	–0.30, –1.2 +4.4	–0.30, –1.2 +5.8
	x > 1 µg/g	1.5	–0.60, –2.3 +0.77	–0.60, –2.3 +2.1	–0.60, –2.3 +4.4	–0.60, –2.3 +5.8

(b) Two servings per week (7 ounces per week, or 28.6 g/day)

			EPA + DHA			
			x ≤ 3 mg/g	3 < x ≤ 8 mg/g	8 < x ≤ 15 mg/g	x > 15 mg/g
		Median	2	5.5	11.5	20
Methylmercury	x ≤ 0.1 µg/g	0.05	–0.04, –0.2 +1.5	–0.04, –0.2 +4.2	–0.04, –0.2 +5.8	–0.04, –0.2 +5.8
	0.1 < x ≤ 0.5 µg/g	0.3	–0.2, –0.9 +1.5	–0.2, –0.9 +4.2	–0.2, –0.9 +5.8	–0.2, –0.9 +5.8
	0.5 < x ≤ 1 µg/g	0.75	–0.6, –2.3 +1.5	–0.6, –2.3 +4.2	–0.6, –2.3 +5.8	–0.6, –2.3 +5.8
	x > 1 µg/g	1.5	–1.2, –4.7 +1.5	–1.2, –4.7 +4.2	–1.2, –4.7 +5.8	–1.2, –4.7 +5.8

(c) Four servings per week (14 ounces per week, or 57.1 g/day)

			EPA + DHA			
			x ≤ 3 mg/g	3 < x ≤ 8 mg/g	8 < x ≤ 15 mg/g	x > 15 mg/g
		Median	2	5.5	11.5	20
Methylmercury	x ≤ 0.1 µg/g	0.05	–0.08, –0.31 +3.1	–0.08, –0.31 +5.8	–0.08, –0.31 +5.8	–0.08, –0.31 +5.8
	0.1 < x ≤ 0.5 µg/g	0.3	–0.48, –1.9 +3.1	–0.48, –1.9 +5.8	–0.48, –1.9 +5.8	–0.48, –1.9 +5.8
	0.5 < x ≤ 1 µg/g	0.75	–1.2, –4.7 +3.1	–1.2, –4.7 +5.8	–1.2, –4.7 +5.8	–1.2, –4.7 +5.8
	x > 1 µg/g	1.5	–2.4, –9.3 +3.1	–2.4, –9.3 +5.8	–2.4, –9.3 +5.8	–2.4, –9.3 +5.8

(d) Seven servings per week (25 ounces per week, or 100 g/day)

			EPA + DHA			
			x ≤ 3 mg/g	3 < x ≤ 8 mg/g	8 < x ≤ 15 mg/g	x > 15 mg/g
		Median	2	5.5	11.5	20
Methylmercury	x ≤ 0.1 µg/g	0.05	–0.14, –0.5 +5.4	–0.14, –0.5 +5.8	–0.14, –0.5 +5.8	–0.14, –0.5 +5.8
	0.1 < x ≤ 0.5 µg/g	0.3	–0.84, –3.3 +5.4	–0.84, –3.3 +5.8	–0.84, –3.3 +5.8	–0.84, –3.3 +5.8
	0.5 < x ≤ 1 µg/g	0.75	–2.1, –8.2 +5.4	–2.1, –8.2 +5.8	–2.1, –8.2 +5.8	–2.1, –8.2 +5.8
	x > 1 µg/g	1.5	–4.2, –16.3 +5.4	–4.2, –16.3 +5.8	–4.2, –16.3 +5.8	–4.2, –16.3 +5.8

a Fish serving size was estimated to be 100 g. Ratio of DHA to EPA + DHA was assumed to be 0.67. Maternal body weight was assumed to be 60 kg. The numbers in red are estimates of IQ points lost from methylmercury exposure, with the lower value of the two values calculated using the central estimate of –0.18 and the higher value calculated using the upper-bound estimate of –0.7. The number in green in each cell is the estimate of IQ points gained from DHA exposure using the coefficient of 4 IQ points for 100 mg of DHA intake. The maximum positive effect from DHA was estimated at 5.8 points. Yellow shaded cells represent the estimates where the net effect on child IQ, using the upper-bound estimate for methylmercury, is negative.

Table 5. Estimated changes in mortality per million people from consuming fish with different dioxin and EPA plus DHA contents [a]

(a) One serving per week (3.5 ounces per week, or 14.3 g/day)

			EPA + DHA							
			x ≤ 3 mg/g		3 < x ≤ 8 mg/g		8 < x ≤ 15 mg/g		x > 15 mg/g	
		Median	2		5.5		11.5		20	
Dioxins	x ≤ 1.0 pg/g	0.2	–50	+4,550	–50	+12,500	–50	+26,200	–50	+39,800
	1.0 < x ≤ 4.0 pg/g	2.5	–600	+4,550	–600	+12,500	–600	+26,200	–600	+39,800
	4.0 < x ≤ 8.0 pg/g	6.0	–1,400	+4,550	–1,400	+12,500	–1,400	+26,200	–1,400	+39,800
	x > 8.0 pg/g	20.0	–4,800	+4,550	–4,800	+12,500	–4,800	+26,200	–4,800	+39,800

(b) Two servings per week (7 ounces per week, or 28.6 g/day)

			EPA + DHA							
			x ≤ 3 mg/g		3 < x ≤ 8 mg/g		8 < x ≤ 15 mg/g		x > 15 mg/g	
		Median	2		5.5		11.5		20	
Dioxins	x ≤ 1.0 pg/g	0.2	–100	+9,100	–100	+25,000	–100	+39,800	–100	+39,800
	1.0 < x ≤ 4.0 pg/g	2.5	–1,200	+9,100	–1,200	+25,000	–1,200	+39,800	–1,200	+39,800
	4.0 < x ≤ 8.0 pg/g	6.0	–2,900	+9,100	–2,900	+25,000	–2,900	+39,800	–2,900	+39,800
	x > 8.0 pg/g	20.0	–9,500	+9,100	–9,500	+25,000	–9,500	+39,800	–9,500	+39,800

(c) Four servings per week (14 ounces per week, or 57.1 g/day)

			EPA + DHA							
			x ≤ 3 mg/g		3 < x ≤ 8 mg/g		8 < x ≤ 15 mg/g		x > 15 mg/g	
		Median	2		5.5		11.5		20	
Dioxins	x ≤ 1.0 pg/g	0.2	–190	+18,200	–190	+39,800	–190	+39,800	–190	+39,800
	1.0 < x ≤ 4.0 pg/g	2.5	–2,400	+18,200	–2,400	+39,800	–2,400	+39,800	–2,400	+39,800
	4.0 < x ≤ 8.0 pg/g	6.0	–5,700	+18,200	–5,700	+39,800	–5,700	+39,800	–5,700	+39,800
	x > 8.0 pg/g	20.0	–19,000	+18,200	–19,000	+39,800	–19,000	+39,800	–19,000	+39,800

(d) Seven servings per week (25 ounces per week, or 100 g/day)

			EPA + DHA							
			x ≤ 3 mg/g		3 < x ≤ 8 mg/g		8 < x ≤ 15 mg/g		x > 15 mg/g	
		Median	2		5.5		11.5		20	
Dioxins	x ≤ 1.0 pg/g	0.2	–330	+31,900	–330	+39,800	–330	+39,800	–330	+39,800
	1.0 < x ≤ 4.0 pg/g	2.5	–4,200	+31,900	–4,200	+39,800	–4,200	+39,800	–4,200	+39,800
	4.0 < x ≤ 8.0 pg/g	6.0	–10,000	+31,900	–10,000	+39,800	–10,000	+39,800	–10,000	+39,800
	x > 8.0 pg/g	20.0	–33,300	+31,900	–33,300	+39,800	–33,300	+39,800	–33,300	+39,800

a Fish serving size was estimated to be 100 g (3.5 ounces). Mean population body weight was assumed to be 60 kg. The numbers in red are estimates of lives lost from dioxin exposure, prepared using upper-bound estimates of risk. The numbers in green are the estimates of lives saved due to reduction in coronary heart disease risk from EPA + DHA intake. The maximum positive effect from EPA + DHA was estimated to occur at 250 mg/day. Yellow shaded cells represent the estimates where the net effect is negative; lives lost are greater than lives saved.

Note that none of the fish species evaluated fell into the maximum dioxin/minimum n-3 PFA category where risk was greater than benefit (see Table 3), and relatively few fish species fell into the mercury range where risk was greater than benefit (see Table 2).

It should be noted that Tables 4 and 5 assume a serving size of 100 grams (3.5 ounces). A study by Smiciklas-Wright et al. (2002) estimated mean and 90th percentile fish meal size for general population adults using data gathered in the 1994–1996 USDA continuing survey of food intakes by individuals. The average amount of finfish (other than tuna) per eating occasion was 114 grams; males, age 40 to 59, had the highest meal size, with a mean of 130 grams (4.6 ounces) and a 90th percentile value of 243 grams (8.6 ounces). Studies of recreational fishers have reported average meal sizes up to 376 grams (13.3 ounces; Burger et al. 1999), while studies of Native American tribal fish consumers also report meal sizes significantly larger than 100 grams.

Concentrations of mercury and dioxins in finfish and shellfish collected in Washington State during the last 10 years are summarized in *Technical Issue Paper: Chemical Contaminants in Dietary Protein Sources*. Average mercury concentrations range from 0.011 to 0.24 µg/g (11 to 240 µg/kg) in Washington state finfish, and from 0.0074 to 0.067 µg/g (7.4 to 67 µg/kg) in Washington state shellfish. Mean dioxin TEQs range from 0.054 to 1.7 pg/g in Washington State finfish; mean concentrations in shellfish range from 0.080 to 6.1 pg/g. These concentrations indicate that consumption of seafood results in a net health benefit.

For example, maternal consumption of 25 ounces per week (or about three 8-ounce servings per week) of seafood contaminated with methylmercury at 0.24 µg/g (the high end of the average concentration in Washington state finfish) would be expected to result in a net increase in child IQ. An estimated 5.4 IQ points would be gained due to DHA exposure, compared to a loss of up to 3.3 IQ points due to methylmercury exposure (Table 4).

Similarly, consumption of 25 ounces per week (or about three 8-ounce servings per week) of seafood contaminated with dioxins/furans at a concentration of 1.7 pg/g TEQ (the high end of the average dioxin concentration in Washington state finfish) would be expected to result in a net increase in health benefits. An estimated 31,900 lives would be saved due to a reduction in coronary heart disease, compared to a loss of up to 4,200 lives due to dioxin toxicity, for each million people exposed (Table 5).

The Expert Consultation[11] summarized a large body of information available on the health benefits and risks associated with fish consumption including:

- Consumption of fish provides energy, protein, and a range of other important nutrients, including the long-chain n-3 polyunsaturated fatty acids (long-chain n-3 PFAs). Optimal health benefits can be maximized by consuming fish with higher long-chain n-3 PFA content and lower methylmercury content. The risk of coronary heart disease mortality is significantly increased by not eating fish.
- The benefits of fish consumption, demonstrated in numerous studies across a wide range of populations, reflect the sum of benefits and risks from all of the constituents in the fish.

[11] Some of the statements taken from the Expert Consultation have been edited here for clarity or brevity.

- Based on observed dose-response relationships and other factors, it is very unlikely that the benefits of fish consumption are explained to any large extent by the replacement of less "healthy" foods with fish. If this were the case, however, it would still represent a causal effect of fish consumption.
- Among the general adult population, consumption of fish, particularly fatty fish, lowers the risk of mortality from coronary heart disease. There is an absence of probable or convincing evidence of risk of coronary heart disease associated with methylmercury. While convincing evidence that high dioxin exposure increases the risk of cancer, there is currently insufficient evidence that typical levels of dietary dioxins (such as seen in fish and other dietary sources) increase the risk of cancer. Potential cancer risks associated with dioxins are well below established coronary heart disease benefits from fish consumption.
- When comparing the benefits of long-chain n-3 PFAs with the risks of methylmercury among women of childbearing age, maternal fish consumption lowers the risk of suboptimal neurodevelopment in their offspring compared with the offspring of women not eating fish in most circumstances evaluated.
- At levels of maternal exposure to dioxins (from fish and other dietary sources) that do not exceed the provisional tolerable monthly intake (PTMI) of 70 pg/kg body weight[12] established by Joint Expert Council (for PCDDs, PCDFs, and coplanar PCBs), neurodevelopmental risk for the fetus is negligible. At levels of maternal exposure to dioxins (from fish and other dietary sources) that exceed the PTMI, neurodevelopmental risk for the fetus may no longer be negligible.
- Among infants, young children, and adolescents, the available data are currently insufficient to derive a quantitative framework of the health risks and health benefits of eating fish. However, healthy dietary patterns that include fish consumption and are established early in life influence dietary habits and health during adult life.

b. Institutes of Medicine (2007)

The National Oceanic and Atmospheric Administration, which regulates U.S. marine fisheries, asked the Institutes of Medicine (IOM) of the National Academies to convene a committee to examine the scientific evidence on the nutritional benefits and risks from seafood. The IOM committee was charged to:

- identify and prioritize adverse health effects from both naturally occurring and introduced toxicants in seafood;
- assess evidence on availability of specific nutrients in seafood compared to other food sources;
- determine the impact of modifying food choices to reduce intake of naturally occurring and introduced toxicants on nutrient intake and nutritional status within the U.S. population;
- develop a decision path for U.S. consumers to balance their seafood choices to obtain nutritional benefits while minimizing exposure risks; and
- identify data gaps and recommend future research.

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[12] By comparison, the USEPA RfD for 2,3,7,8-TCDD is 0.7 pg/kg/day, or roughly 210 pg/kg/month assuming a 30-day month.

The IOM committee concentrated on issues affecting marine species and published its final report in 2007 (Nesheim and Yaktine 2007).

For the benefit/risk analysis, the IOM committee evaluated changes in benefits and risks associated with changing consumption patterns that may occur as a result of guidance provided to consumers regarding fish consumption. The IOM committee examined the impact of food-choice trade-offs involving calories, saturated fat, EPA/DHA, selenium, and iron. Contaminants evaluated, due to availability of data, were methylmercury, dioxins, and dioxin-like compounds. This information was used to develop guidance on seafood consumption tailored to four distinct population groups: (1) females who are or may become pregnant or who are breastfeeding; (2) children up to age 12; (3) adolescent males, adult males, and females who will not become pregnant; (4) adult males and females who are at risk of cardiovascular disease.

Seafoodhealthfacts.org, a joint project of Oregon State University, Seafood Consumer Center, Cornell University, and the Universities of California, Delaware, Florida, and Rhode Island, modified one of the sample public risk communication graphics from the IOM report when it created a seafood health reference guide for healthcare providers (Seafoodhealthfacts.org, undated). The Seafoodhealthfacts.org figure includes the FDA action level for mercury, which puts the mercury content of the various seafood species into context (Figure 2). This figure shows estimated n-3 PFA intake (as EPA + DHA) in a 3-ounce serving of fish against the average mercury levels for each species. Those species considered to be low risk for mercury exposure are colored green. Yellow species have high average mercury levels that exceed or approach the FDA action level of 1 part per million (ppm, or mg/kg) and should be avoided by sensitive groups (women who may become pregnant, pregnant and breastfeeding women, and young children) according to recommendations by several groups (USFDA, USEPA, IOM, etc.). The blue colored species (canned albacore tuna) is considered a good source of n-3 PFAs but consumption should be limited due to mercury levels in this species.

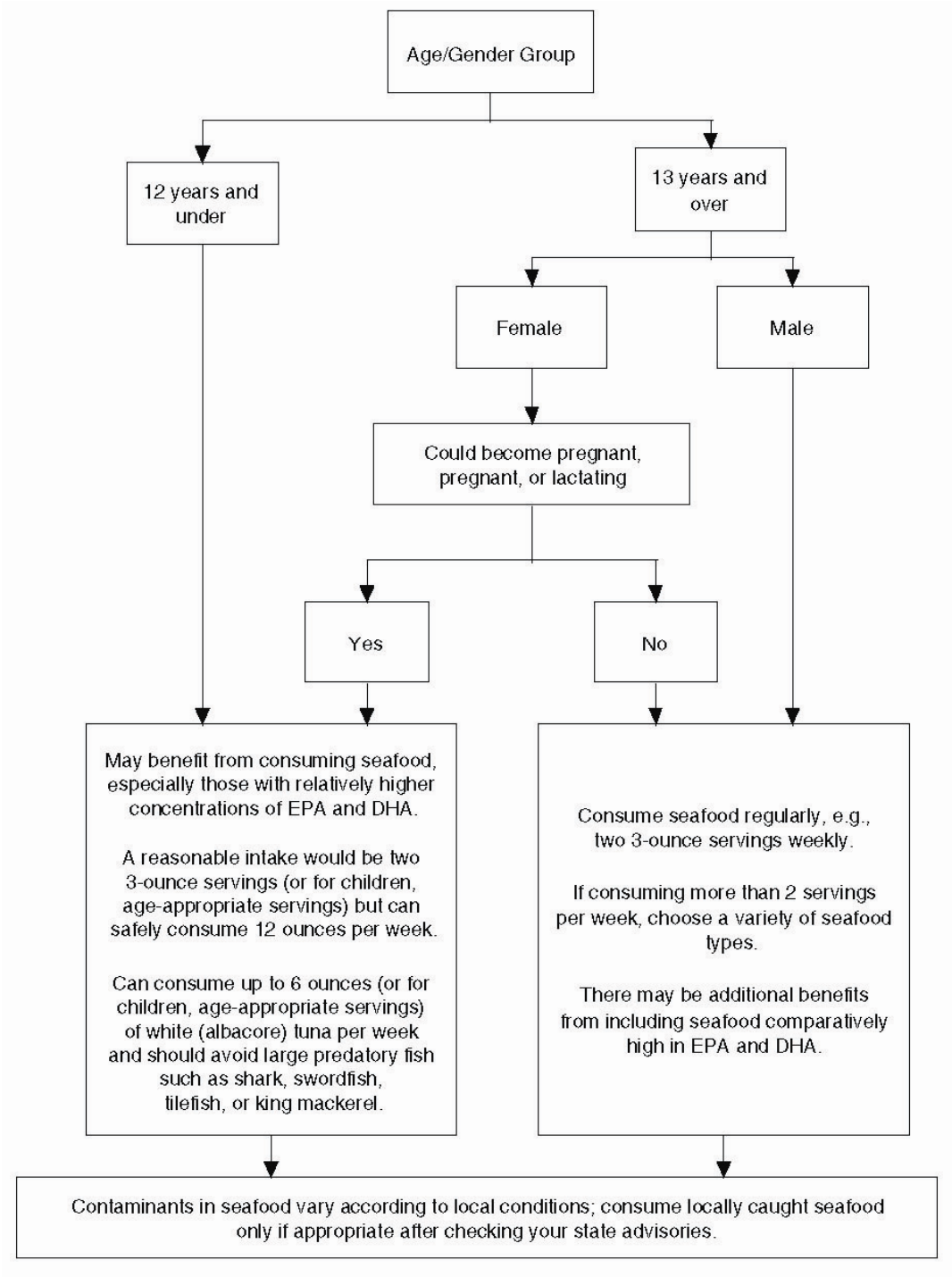

Figure 1. Decision pathway representing the balance between benefits and risks associated with seafood consumption (Source: Nesheim and Yaktine 2007)

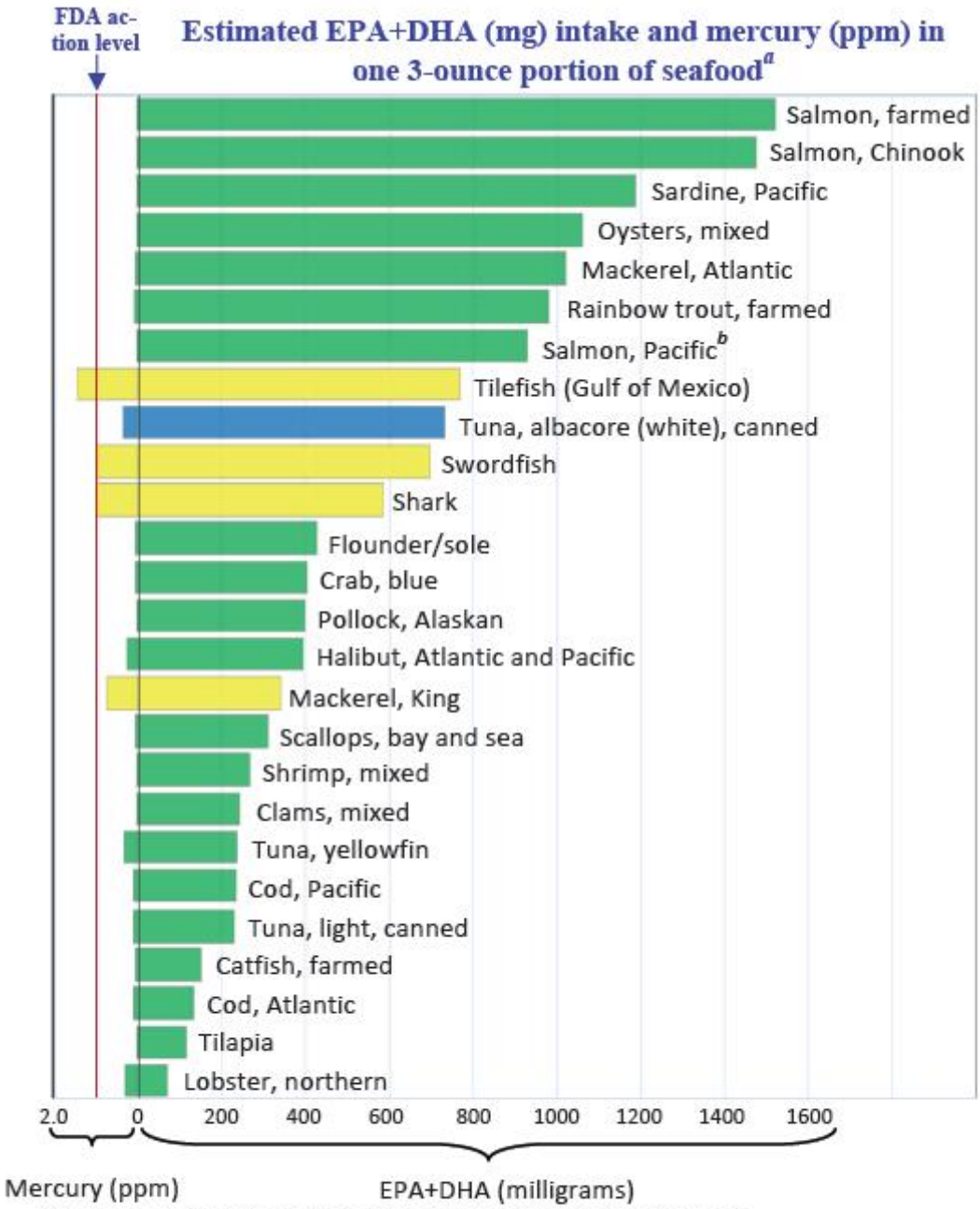

Figure 2. EPA+DHA and mercury content in representative seafood portions. Source: Seafoodhealthfacts.org.

c. USEPA/TERA (1999)

The USEPA and Toxicology Excellence for Risk Assessment (TERA) summarized what was known about health benefits and risks from fish consumption in a report published in 1999. The report compared the possible health risks of consuming contaminated fish while considering the potential health benefits lost by not eating fish, and proposed a framework for comparing the benefits and risks quantitatively.

Benefits described by the USEPA/TERA report included discussions of the beneficial protein, fatty acid profiles, and nutrients provided by fish and the various studies to date on CHD and heart attack, and other health endpoints which have been described in detail in Section II. At the time, however, the authors believed further study was needed to resolve whether fish consumption provided significant protection against CHD or heart attack. Contaminants considered included DDT (an organochlorine pesticide now banned in the United States) and its metabolites, methylmercury, dioxin, PCBs, chlordane (an organochlorine pesticide now banned in the United States), and chlorpyrifos (an organophosphate pesticide).

The USEPA/TERA report concluded that consuming uncontaminated fish (or at least fish that are smaller, younger, or in general less contaminated) may provide health benefits, but without the potential health risks associated with contamination. Before eating any contaminated fish, consumers should consider fish supplies from cleaner water bodies, eating smaller, less contaminated fish, and cooking and cleaning methods that reduce contaminants. The eating of such “cleaner” fish rather than more contaminated fish would maximize the net benefit of fish consumption. However, better estimations of benefits were needed for the general population and its sensitive subgroups and that better risk information is needed on the chemicals that commonly contaminate fish. The data gaps identified were sufficiently large so as to prevent any definitive conclusions from the study or any overall recommendations regarding existing fish consumption advisory programs of the United States or other countries. The authors believed further study was needed to confirm and extend these preliminary findings.

Conclusions

For those who consume meats, replacing meats with vegetable alternatives (e.g., beans) or fish is one strategy to replace saturated fats with monounsaturated fats and reduce cholesterol (Lichtenstein et al. 2006; USDA and USDHHS 2010). Increasing seafood consumption of most species will lead to increased n-3 PFA intake and reduced risk for major health conditions such cardiovascular and coronary heart disease. Health benefits associated with consumption of fish, particularly fatty fish such as salmon, are well documented.

While exposures to methylmercury and persistent organic pollutants may have negative human health impacts, there are considerable uncertainties about estimates of these health risks to the general population at levels present in commercially obtained seafood (Nesheim and Yaktine 2007).

High rate fish consumers such as certain ethnic groups (Japanese, American Indian) can accumulate mercury levels that approach or exceed reference doses (Tsuchiya et al. 2008).

However, Mahaffey et al. (2008) suggest that data on methylmercury and n-3 PFA concentrations seafood can be used to guide the selection of individual fish and shellfish species that are higher in n-3 PFA and low in methylmercury content (see Figure 2), thereby reducing mercury exposure. Further, the risks from lipophilic compounds can be reduced by trimming fat, using cooking methods that reduce fat such as broiling, and by eating a variety of species.

A recurrent theme in recent reviews and analyses is that reducing fish consumption can negatively impact the health status of vulnerable populations (Dórea 2008). The evidence suggests that the fetus and infants may be among the principal beneficiaries from certain nutrients in seafood. Few data are available about the extent to which beneficial components of seafood, such as selenium and omega-3 fatty acids, might mitigate risks associated with contaminants in seafood (Nesheim and Yaktine 2007).

Where there are local instances of excessively high levels of contaminants such as PCBs in recreationally caught fish, it is important that consumers, especially those in sensitive populations, consult with their local health department before consuming locally-caught fish.

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