

1 Selenium Health Benefit Values Provide a Reliable Index of Seafood Benefits vs. Risks

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26 Abbreviations:

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28 Health Benefit Value, HBV

29 Mercury, Hg

30 Methylmercury, CH<sub>3</sub>Hg

31 Mercury selenide, HgSe

32 Parts per million, ppm

33 Polychlorobiphenyls, PCB

34 Selenium, Se

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39 Keywords:

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41 Selenium, mercury, fish, seafood, brain.

42

43 **Abstract**

44

45 **Background:** Methylmercury (CH<sub>3</sub>Hg) toxicity causes irreversible inhibition of selenium (Se)-dependent  
46 enzymes, including those that are required to prevent and reverse oxidative damage in the brain. Fish  
47 consumption provides numerous essential nutrients required for optimal health, but is also associated with  
48 CH<sub>3</sub>Hg exposure risks, especially during fetal development. Therefore, it is necessary to assess the  
49 amounts of both elements in seafood to evaluate relative risks or benefits. Consumption of ocean fish  
50 containing Se in molar excess of CH<sub>3</sub>Hg will prevent interruption of selenoenzyme activities, thereby  
51 alleviating Hg-exposure risks. Because dietary Se is a pivotal determinant of CH<sub>3</sub>Hg's effects, the  
52 Selenium Health Benefit Value (HBV) criterion was developed to predict risks or benefits as a result of  
53 seafood consumption. A negative HBV indicates Hg is present in molar excess of Se and may impair Se  
54 availability while a positive HBV indicates consumption will improve the Se status of the consumer, thus  
55 negating risks of Hg toxicity.

56 **Objective:** This study examined the Hg and Se contents of varieties of seafood to establish those with  
57 positive HBV's offering benefits and those having negative HBVs indicating potential consumption risks.

58 **Methods:** The Hg and Se molar concentrations in samples of meat from pilot whale, mako shark, thresher  
59 shark, swordfish, bigeye tuna, and skipjack tuna were used to determine their HBV's in relation to body  
60 weight.

61 **Results:** The HBVs of pilot whale, mako shark, and swordfish were typically negative and inversely  
62 related to body weight, indicating their consumption may impair Se availability. However, the HBV's of  
63 thresher shark, bigeye tuna, and skipjack tuna were uniformly positive regardless of body weights,  
64 indicating their consumption counteracts Hg-dependent risks of selenoenzyme impairment.

65 **Conclusions:** The HBV criterion provides a reliable basis for differentiating seafoods whose intake  
66 should be limited during pregnancy from those that should be consumed to obtain health benefits.

67

## 68 **1.0 Introduction**

69 Selenium (Se) is an essential trace element that is required for synthesis of selenocysteine (Sec), the 21<sup>st</sup>  
70 genetically encoded amino acid required for the activities of selenoenzymes with critical roles in fetal  
71 brain development, growth, thyroid hormone metabolism, calcium regulation and prevention/reversal of  
72 oxidative damage.<sup>1-8</sup> The importance of Se for brain functions is emphasized by the fact that highly  
73 conserved mechanisms have evolved to maintain optimal brain Se concentrations even when dietary Se  
74 intakes are deficient. Because the brain is preferentially supplied,<sup>9-11</sup> its Se concentrations are maintained  
75 near normal (~1  $\mu\text{M}$ ) even when prolonged exposures to Se-deficient diets diminish Se concentrations in  
76 somatic tissues such as blood or liver to ~2% of their normal levels.<sup>2</sup>

77 Numerous studies have shown dietary Se counteracts methylmercury ( $\text{CH}_3\text{Hg}$ ) toxicity<sup>12-18</sup> and  
78 the protective effect of Se from ocean fish consumption against  $\text{CH}_3\text{Hg}$ , toxicity has been repeatedly  
79 shown in laboratory animals.<sup>19-24</sup> Serious impairments of brain Se and selenoenzyme activities are only  
80 known to occur as a result of genetic knockouts of Se-transport/uptake proteins<sup>10, 25-26</sup> or following high  
81  $\text{CH}_3\text{Hg}$  exposures.<sup>24, 27, 28</sup> The ability of Se to decrease or abolish the toxic effects of high Hg exposures  
82 has been well established<sup>29-32</sup> and it is now understood that the mechanism of  $\text{CH}_3\text{Hg}$  toxicity primarily  
83 occurs through disruption of brain Se metabolism.<sup>5, 33-38</sup> Prior to recognition of  $\text{CH}_3\text{Hg}$ 's role in inhibiting  
84 selenoenzyme metabolism, the mechanism of  $\text{CH}_3\text{Hg}$  toxicity was thought to involve its high affinity for  
85 thiols ( $10^{39}$ ) and arise due to disruption of sulfur metabolism. Sulfur is far more abundant in tissues than  
86 Se (~300,000:1), but Hg's association constant for Se ( $10^{45}$ ) is ~1 million times higher than its affinity for  
87 sulfur.<sup>39</sup> Due to their high tissue concentrations, thiomolecules bind  $\text{CH}_3\text{Hg}$  initially, but because they are  
88 substrates for selenoenzymes, they directly deliver  $\text{CH}_3\text{Hg}$  into enzyme's active site in the proper  
89 orientation to bring the Hg moiety into close proximity with the Se of the catalytic Sec residue. The  
90  $\text{CH}_3\text{Hg}$  transfers from the thiol to the Sec, forming a  $\text{CH}_3\text{Hg}$ -Sec which is degraded into Hg selenide  
91 ( $\text{HgSe}$ ), a virtually insoluble (solubility constant  $10^{-58}$  to  $10^{-65}$ ) and therefore biologically unavailable form  
92 of Se,<sup>39</sup> which can contribute to a functional Se deficiency if Hg sequestration rates outpace Se transport  
93 into the tissue.

94 An important aspect of dietary  $\text{CH}_3\text{Hg}$  is its ability to cross placental and blood-brain barriers to  
95 irreversibly inhibit selenoenzyme activities in the fetal brain.<sup>27, 28, 42</sup> Therefore, high  $\text{CH}_3\text{Hg}$  exposures  
96 during pregnancy are a concern if dietary Se intakes are not adequate to offset losses due to Hg  
97 sequestration. Maternal  $\text{CH}_3\text{Hg}$  exposures from eating seafoods with high Hg:Se molar ratios such as  
98 certain types of shark<sup>43</sup> or pilot whale meats and blubber<sup>44-47</sup> have been reported as having subtle adverse  
99 effects on child neurodevelopment. Conversely, maternal consumption of ocean fish that contain more Se  
100 than Hg has not been associated with health risks, but instead offers health benefits.<sup>48-57</sup> With few  
101 exceptions, ocean fish contain more Se than Hg<sup>58</sup> and are abundant sources of important nutrients

102 required for fetal development.<sup>48,49,59</sup> Therefore, since most ocean fish are rich sources of dietary Se, there  
103 is protection against the CH<sub>3</sub>Hg they contain.

104 The Health-Benefit-Value (HBV) indicates the relative molar contents of Se and Hg that are  
105 present in a food.<sup>36,41,58,60</sup> Most seafoods have positive HBV's indicating Se is present in molar excess of  
106 their CH<sub>3</sub>Hg contents, while negative values indicate they contain CH<sub>3</sub>Hg in excess of Se.<sup>58,61</sup> For  
107 example, pilot whale muscle meat samples have Hg contents (3.31 µg/g; 16.4 µmol/kg) that are far higher  
108 than their Se (0.25 µg/g; 3.1 µmol/kg) concentrations (Hg:Se molar ratios ~5:1).<sup>62</sup> Since these results are  
109 from the 1977 pilot whale data set which was used to estimate maternal Hg exposures in the Faroe  
110 Islands,<sup>44</sup> (the population study which was used to establish maternal seafood consumption advice) it is  
111 important to compare the Hg and Se contents of pilot whales to representative varieties of ocean fish. To  
112 establish reference ranges of positive and negative HBV seafoods in relation to their body weights, this  
113 study compared the molar concentrations of Hg and Se in pilot whale, mako shark, thresher shark,  
114 swordfish, bigeye tuna, and skipjack tuna muscle meats.

115

## 116 **2.0 Methods:**

117 Because shark and pilot whale meats were the dominant source of Hg in studies which reported finding  
118 harmful effects, this study compared their HBVs to those of a selection of commonly consumed varieties  
119 of ocean fish. The ocean fish data evaluated in this study are from samples of edible fish portions  
120 collected in 2006 from commercial landings of pelagic fish as reported in Kaneko and Ralston.<sup>58</sup> Briefly,  
121 fish harvested from the central Pacific were weighed and 100 g samples of edible muscle from the  
122 anterior portion of the dorsal muscle mass were stored frozen in trace metal free plastic bags. Chain of  
123 custody was maintained from the time the samples were collected until they were analyzed for Hg and Se.  
124 Sample aliquots of ~0.4 g (wet weight) weighed to 0.0001 g from each sample were transferred into  
125 single use trace element free 50 mL digestion tubes (Environmental Express, Mt Pleasant, SC 29464)  
126 with every tenth fish sample being prepared in duplicate and with elemental spike recovery samples being  
127 performed accompanying each batch. Each digestion batch was processed with blank and certified  
128 standard reference materials (dogfish muscle certified reference material DORM-2, National Research  
129 Council of Canada, Ottawa, Ontario Canada). Samples were treated with 5 mL of 16N nitric acid (Fisher  
130 Trace Metal Grade, Fisher Scientific, www.fishersci.com) and heated at 85°C in deep cell hot blocks  
131 (Environmental Express, Mt. Pleasant, SC) for 24 hours in capped tubes. Samples were cooled and 1.5  
132 mL of 30% H<sub>2</sub>O<sub>2</sub> (Fisher Certified A.C.S., Fisher Scientific, www.fishersci.com) was added and samples  
133 were recapped and returned to heating in the dry block at 85°C. Samples were cooled and 15 mL of 12N  
134 HCl (Fisher Trace Metal Grade, Fisher Scientific, Fisher Scientific, www.fishersci.com) were added.  
135 Samples were heated at 90°C for 90 minutes to reduce Se-VI to Se-IV, then cooled and diluted to 50 mL

136 with double distilled water. Samples were analyzed for Hg content by cold vapor atomic absorption  
 137 spectrophotometry using a CETAC M-6000A (CETAC Technologies Inc, Omaha, NE), and Se was  
 138 analyzed by hydride generation atomic fluorescence spectroscopy using a PS Analytical Dual Millennium  
 139 Excalibur, (PS Analytical, Deerfield Beach, FL). The Hg and Se molar concentrations of these samples  
 140 were used to calculate their HBV's and Se deficits or excess were evaluated in relation to body weights.

141 The large sizes of pilot whales (*Globicephala melas*) precluded weighing to establish body mass.  
 142 As reported in the original literature,<sup>62</sup> their mass was recorded on the basis of “skinns” (a traditional  
 143 apportionment term) rather than body weights. A 75 kg skinn corresponds to ~50 kg of meat and ~25 kg  
 144 of blubber along with varying amounts of liver and kidney corresponding to an estimated intake ratio of  
 145 65:32:3 for muscle meat, blubber, and liver respectively; the amount of kidney consumed was not  
 146 reported.<sup>63</sup> Male pilot whales have a maximum body weight of ~2300 kg and females are up to ~1300  
 147 kg.<sup>64</sup> Therefore, to estimate pilot whale body weights, the number of skinns per whale was multiplied by  
 148 1.9; a factor that was determined to provide approximations that conform with their normal weight range.  
 149 This resulted in a mean estimated adult body weight of ~1187 kg, with the largest whale having a value of  
 150 2280 kg, values which correspond to reference weights reported for this species.

151 The Hg and Se mass concentrations (mg/kg) were converted to molar concentrations ( $\mu\text{mole/kg}$ ),  
 152 and results were evaluated. The concentrations of Hg and Se in individual fish and whale meat samples  
 153 were used to calculate corresponding HBVs using the equation described in Ralston et al., 2016:<sup>35</sup>

$$154 \quad \text{HBV} = (\text{Se} - \text{Hg})/\text{Se} \cdot (\text{Se} + \text{Hg}) \quad (\text{Equation 1.})$$

156  
 157 The molar excess of Se (“free” Se) present in the samples was determined by subtracting the molar Hg  
 158 concentration from the molar Se concentration for individual samples. Means and standard deviations of  
 159 elemental molar concentrations, HBV's, and Se excess or deficits were calculated, graphed, and  
 160 evaluated.

### 162 **3.0 Results:**

163 The reference material used for Hg and Se in fish tissue was (DORM-2) dogfish (freeze dried powdered  
 164 *Squalus acanthias*) muscle obtained from the National Research Council of Canada, with reference values  
 165 of  $1.40 \pm 0.09 \mu\text{g Se/g}$  and  $4.47 \pm 0.32 \mu\text{g Hg/g}$  (dry weight basis). We observed that Hg recovery was  
 166 inversely related to the amount of sample digested ( $p = 0.05$ ),  $F = 6.91$ , Adjusted  $R^2 = 0.54$ . While 100  
 167 mg (or less) of DORM-2 provided recoveries of ~99.9%, Hg recoveries declined as the amount of sample  
 168 increased. For example; 150 mg provided a recovery of  $95.4 \pm 0.2\%$  and 200 mg provided a recovery of  
 169  $90.8 \pm 0.7\%$ . This effect was not observed for Se recoveries from DORM-2. Additionally, inclusion of

170 HCl in addition to HNO<sub>3</sub> in a quantity approximating aqua regia proportions was essential for complete  
171 recoveries. The observed Se ( $1.36 \pm 0.04$  ug/g;  $97 \pm 3\%$  of certified value), and Hg contents ( $4.32 \pm 0.38$   
172 ug/g;  $97 \pm 9\%$  of certified value) indicated the elemental recoveries were reliable and replicate sample  
173 analyses indicated adequate precision. While digestion blank values for Hg were sufficiently low to be  
174 considered negligible, digestion blank Se contents ( $0.49 \pm 0.17$  ng/ml) were subtracted prior to calculating  
175 Se contents of samples.

176

### 177 *3.1 Pilot whales*

178 The Hg contents of pilot whale meats uniformly exceeded Se contents on a molar basis in adult animals  
179 (Fig. 1, Fig. 3, Table 2). The amount of Hg increased in direct relation to body size (See Table 1 and Fig.  
180 1). Aside from the higher Se contents noted in fetal pilot whales (not shown) and very young calves, total  
181 Se contents were not associated with body size (Fig. 2). This is consistent with previous findings that  
182 homeostatic controls regulate tissue Se, thus body size does not typically affect the amount of Se present,  
183 although HgSe accumulation can increase in certain tissues.<sup>65</sup> Aside from samples of one adult and two  
184 young calves, the HBV's of pilot whale meat were negative and significantly diminished ( $p = 0.01$ ;  $F =$   
185  $9.1$ ) as body size increased (Fig. 2, Table 2). Since Hg bioaccumulation was directly associated with body  
186 size of pilot whales (Fig. 3), the calculated Se-deficit associated with these samples was directly related to  
187 their Hg contents ( $p < 0.01$ ;  $F = 12.7$ ). Males of this species live up to ~40 years and attain maximal  
188 weights of ~2,300 kg while females live up to 60 years and attain maximal weights of ~1,300 kg.<sup>64</sup>  
189 Although the sex of the assessed samples was not available, this sexual dimorphism may be evident in the  
190 Hg accumulation and HBV distribution patterns noted in pilot whales (Figures 1 and 2).

191

### 192 *3.2 Mako sharks*

193 The Hg contents of mako shark were directly related to their body size (Table 1, Fig. 2). The HBV of all  
194 samples included in this assessment were uniformly negative (Fig. 2, Table 2). Although the HBV of  
195 these samples tended to decline as body size increased, the relationship was not significant ( $p = 0.11$ ),  
196 possibly because only 10 samples were assessed and the range of sample body weights examined was  
197 relatively narrow (40-80 kg). However, like pilot whales, mako shark meat contained more Hg than Se,  
198 and Se-deficits (Fig. 3) were directly associated with increasing Hg contents ( $p < 0.001$ ;  $F = 139.9$ ).

199

### 200 *3.3 Swordfish*

201 The Hg contents of swordfish were directly related to body size (Fig. 1). Although the HBV of the  
202 swordfish was positive in many specimens, many samples had negative values (Fig. 2) and there was a  
203 tendency for HBV's to decline in relation to increasing size ( $p = 0.07$ ). As a result, the average HBV for

204 swordfish was ~zero, but highly variable (Fig. 2, Table 2). The Se surplus or deficit was dependent on Hg  
205 content ( $p < 0.001$ ;  $F = 38.5$ ), with samples containing Hg in excess of  $5 \mu\text{mol/kg}$  ( $\sim 1 \text{ mg/kg}$ ) having the  
206 lowest HBV's (Fig. 3).

207

### 208 *3.4 Thresher sharks*

209 The Hg contents in thresher shark tended to increase in relation to increasing body size (Fig. 1) but Se  
210 contents were consistently higher in all samples assessed (Fig. 2, Table 2). As a result, the HBV of  
211 thresher shark samples were uniformly positive although they declined with increasing body size due to  
212 increasing Hg (Fig. 2). Therefore, unlike mako shark, thresher shark meats provide a Se-surplus.

213

### 214 *3.5 Bigeye tuna*

215 The Hg contents of bigeye tuna samples were lower than those observed in pilot whale, shark or  
216 swordfish (Fig. 1, Table 1). Although their Hg concentrations were directly related to body size (Fig. 1,  
217 Table 1), Se contents were higher than Hg in all samples assessed (Fig. 3, Table 2). As a result, their HBV  
218 values were uniformly positive (Fig. 2, Table 2). There was a gradual decline in surplus Se ( $p = 0.01$ ;  $F =$   
219  $6.8$ ) associated with increasing Hg concentrations, but the values were consistently positive (Fig. 3).

220

### 221 *3.6 Skipjack tuna*

222 The Hg contents of skipjack tuna were low in comparison to other species assessed in this study and not  
223 related to body size (Fig. 1, Table 1). The levels of Se in their tissues were variable and unrelated to body  
224 size (Fig. 2). The red meat of skipjack tuna had considerably higher Se contents than the lighter muscle  
225 mass (data not shown). The source of this variability is unknown and was not observed in any other  
226 varieties of ocean fish studied. The HBV of skipjack tuna were uniformly positive and independent of  
227 size (Fig. 2, Table 2). The Se-surplus was not significantly related to Hg or Se concentrations.

228

## 229 **4.0 Discussion:**

230 Ocean fish consumption during pregnancy is consistently associated with neurodevelopmental  
231 benefits in children compared to those of mothers that avoid fish consumption.<sup>48-57, 68</sup> Ocean fish are rich  
232 sources of dietary Se,<sup>65</sup> and although Se contents vary considerably between species, it is generally  
233 independent of fish size. However,  $\text{CH}_3\text{Hg}$  concentrations in ocean fish are directly related to their trophic  
234 level, age, size, and can vary by orders of magnitude, negatively affecting their HBV (Fig. 2). As shown  
235 in Fig. 1, Hg bioaccumulation during early growth is minimal, so HBVs are the highest in the youngest  
236 fish (Fig. 2). As their Hg burdens increase, HBV's gradually decline so those with the lowest values tend  
237 to be the oldest and largest of their species (Fig. 2). Although the HBV remains positive in even the

238 largest of most fish species,<sup>58</sup> our results indicate this is not the case for pilot whale, mako shark, or  
239 swordfish (see Table 1, Fig. 3).

240 Seafood consumption advisories currently fail to consider Se, and instead of being based on  
241 studies that examined the effects of ocean fish consumption, are based on studies of the effects of Hg  
242 exposures which primarily originated from consuming pilot whales, not fish. In the Faroe Islands Study,  
243 participant consumption of pilot whale meat, blubber, and liver (in proportions ~65:32:3<sup>63</sup> were the source  
244 of ~85% of their overall Hg exposures,<sup>44,61</sup> The livers (and kidneys) had extremely high Hg and cadmium  
245 contents and whale blubber also contained high concentrations of PCB's and all other persistent  
246 bioaccumulative toxicants.<sup>62,63</sup> Based on the unusually negative HBV of the pilot whale meat, adverse  
247 effects would be expected in children born to mothers who ate pilot whale meat during pregnancy.  
248 However, the Hg-dependent Se losses were offset by Se from the ocean fish also consumed, thus  
249 alleviating adverse consequences and significant improvements in health outcomes were observed in  
250 children whose mothers consumed increasing amounts of ocean fish.<sup>67</sup> These benefits are likely due to Se-  
251 restoration along with other positive effects of ocean fish nutrients required for optimal fetal  
252 neurodevelopment.<sup>48,49,54,55,57,68</sup>

253 In addition, studies of ocean fish consuming populations have found the children of mothers who  
254 ate the most fish during pregnancy had significantly improved neurodevelopmental scores in comparison  
255 to those whose mothers ate no fish.<sup>48,49,54,55,57,68</sup> Children in the US whose mothers avoided fish  
256 consumption during pregnancy lost IQ benefits<sup>53</sup> that were 60-100 times greater<sup>60</sup> than the worst-case  
257 effects reported with Hg exposures from pilot whale consumption in the Faroes. Maternal seafood intake  
258 during pregnancy of less than the amount recommended by the 2004 U.S. fish consumption advisory<sup>69</sup>  
259 (340 g per week) was associated with increased risk of their children being in the lowest quartile for  
260 verbal intelligence quotient (IQ) compared with mothers who consumed more than 340 g per week. Low  
261 maternal seafood intake was also reported to be associated with increased risk of suboptimum outcomes  
262 for prosocial behaviour, fine motor, communication, and social development scores. The authors also  
263 stated that for each outcome measure, the lower the intake of seafood during pregnancy, the higher the  
264 risk of suboptimum developmental outcome.<sup>48</sup> Diminished fish consumption also increased children's  
265 risks for pathological scores in fine motor, communication, and social skills. Conversely, increasing  
266 maternal fish consumption beyond the reference dose during pregnancy was associated with improved  
267 child performance.<sup>48</sup>

268 To ensure the safety of the most sensitive population subgroups, recommendations based on the  
269 HBV criterion are exceedingly cautious in that it considers only the seafood itself, without regard to other  
270 Se sources in the diet. Recognizing that dietary intakes account for ~19.8% of the total variation in  
271 maternal blood Hg concentrations<sup>70</sup> while diet is the exclusive source of Se, the margin of safety afforded



272 by the HBV is purposefully cautious. It does not reflect the amounts of Hg bound to other elements or  
273 consider the other sources of Se in the diet. Since seafood consumers generally eat a variety of fish which  
274 have positive HBV's and enrich their Se intakes, occasional consumption of a negative HBV seafood is  
275 unlikely to diminish Se-status. This may explain why the Faroe Islands study found the effects of high  
276 maternal Hg exposures from consumption of even extraordinarily contaminated seafoods such as pilot  
277 whale meat, blubber, and liver were only associated with subtle diminishments in their children's  
278 subsequent performance assessments.<sup>67</sup> Children in the Faroes had cord blood Hg concentrations as high  
279 as 1  $\mu\text{M}$ , a concentration which has been associated with adult Hg toxicity<sup>71</sup> and not coincidentally,  
280 ~equimolar with the average concentration of Se in most body tissues. Maternal fish consumption was  
281 highly protective against the effects of Hg exposure in the Faroes,<sup>67</sup> and ocean fish provided ~80% of  
282 their dietary Se.<sup>61</sup> This is fortunate since otherwise fetal Se-status among those with high pilot whale meat  
283 consumption would have been grossly impaired. Since ocean fish are among the richest dietary sources of  
284 nutrients with important roles in brain health and development, including Se, long-chain omega-3 fatty  
285 acids, and vitamin D, it is not surprising that increased maternal fish consumption correspond with  
286 improved fetal outcomes.

287         The U.S. Environmental Protection Agency and the U.S. Food and Drug Administration advisory  
288 regarding fish consumption for children and pregnant women<sup>72</sup> includes a chart of >60 types of fish and  
289 shellfish that women and children are encouraged to eat up to 3 servings per week depending on species.  
290 Nearly 90% of fish eaten in the U.S. fall into this "best choices" category, and these recommendations are  
291 consistent with positive HBV's based on their high Se contents relative to Hg. The advisory's "choices to  
292 avoid" category includes: shark, swordfish, king mackerel and tilefish from the Gulf of Mexico, orange  
293 roughy, marlin, and bigeye tuna. The present study found that mako sharks and large swordfish have  
294 negative HBVs which generally coincides with the Hg-based criteria used to establish EPA/FDA  
295 categories. However, thresher sharks had uniformly positive HBV's. Considering there are more than 400  
296 shark species and the advisory does not differentiate among them, more work should be done to assess the  
297 HBV's of commonly consumed shark varieties to segregate those with positive vs. negative HBV's. The  
298 HBV's of king mackerel, tilefish, and orange roughy have not been assessed, but considering their high  
299 Hg contents, maternal consumption of these varieties should be limited until assessments have been  
300 performed. In contrast to the advisory, we find the uniformly positive HBV's of bigeye tuna (HBV = 11.5  
301  $\pm$  3.8; see Table 2), and marlin (HBV = 11.5  $\pm$  4.2 for blue marlin, 8.0  $\pm$  3.2 for striped marlin;  
302 unpublished data), indicate their Hg contents are unlikely to be problematic and should not be a basis for  
303 inclusion in the "choices to avoid" category. Criteria based on fish Hg contents alone lack merit because  
304 they include only half the information required to differentiate Hg-exposure risks from nutritional benefits  
305 of seafood consumption.

306 It is important to point out that the amount of Se in the food web of freshwater bodies and  
307 estuaries can vary depending on Se availability in their watersheds. Thus, the CH<sub>3</sub>Hg and Se levels in  
308 freshwater fish can differ considerably. Bioaccumulation of CH<sub>3</sub>Hg in piscivorous freshwater fish is  
309 inversely related to Se bioavailability.<sup>74-80</sup> Fish from regions with poor soil Se levels (e.g., in Finland,  
310 Canada, South America) will tend to have increased CH<sub>3</sub>Hg contents and lower HBV's. Since Se-status  
311 of remote populations in Se-poor regions is likely to be low, Hg exposure risks may be exacerbated in  
312 subsistence fish consumers.<sup>60</sup> The current EPA freshwater fish advisories are based solely on Hg levels  
313 and vary from state to state. However, like ocean fish, freshwater fish from most North American  
314 watersheds generally contain significantly more Se than Hg<sup>81,82</sup> and therefore have positive HBV's. This  
315 suggests that many water bodies currently listed as "impaired" based on fish Hg contents may need to be  
316 reevaluated. In contrast, the low Se levels which tend to be common in high-Hg freshwater fish from Se-  
317 poor watersheds may indicate accentuated Hg-related risks which are currently being overlooked. This is  
318 especially true of subsistence fish consumers whose locally-sourced foods may also be Se poor would be  
319 at greatest risk from eating fish with negative HBVs. Therefore, freshwater fish and other foods which  
320 may contain high concentrations of Hg and other metallic or organic electrophiles should be evaluated  
321 using HBV criteria to identify populations that are increased at-risk and enhance the reliability of future  
322 risk assessments.

323

#### 324 **4.1 Conclusions:**

325 It is more rational to base maternal seafood consumption advice on the outcomes of studies of  
326 ocean fish eating populations than on the effects of exposures to toxicants which were predominantly  
327 from eating pilot whale meat, organs, and blubber. As previously observed with the majority of other  
328 ocean fish species, this study found skipjack tuna has a uniformly positive HBV that indicates it is safe  
329 and beneficial to eat. Since the HBV's of bigeye tuna, marlin, and thresher shark were also uniformly  
330 positive, they should not be considered "choices to avoid". While the negative HBV of mako sharks and  
331 large swordfish superficially aligns with the FDA/EPA "choices to avoid" category, suggesting avoidance  
332 may be inappropriate since most consumers fail to distinguish between different types of fish and many  
333 over-react to food-safety warnings. Therefore, to minimize risk of harm while optimizing fetal/infant  
334 neurodevelopment, the most prudent advice is to encourage maternal consumption of a variety of ocean  
335 fish with emphasis on those with positive HBV's.

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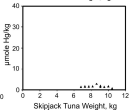
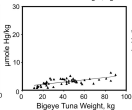
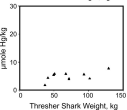
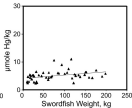
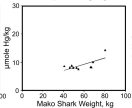
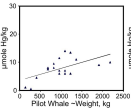
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(6 graphs comparing Hg contents of different seafoods)

Fig. 1. Total Hg concentrations ( $\mu\text{mol/kg}$ ) for the seafoods assessed in this study.

$\mu\text{mole Hg/kg}$

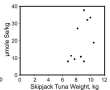
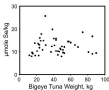
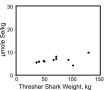
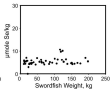
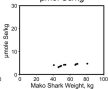
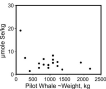
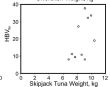
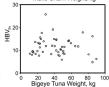
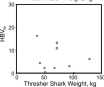
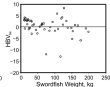
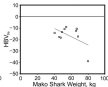
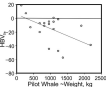


(6 graphs comparing Se contents of different seafoods)

And

(6 graphs comparing  $HBV_{Se}$  of different seafoods)

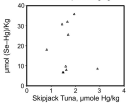
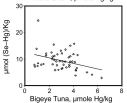
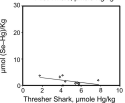
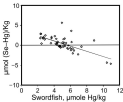
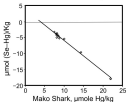
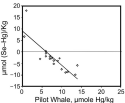
Fig. 2. Total Se concentrations ( $\mu\text{mol/kg}$ ), and calculated HBVs for the seafoods studied.

$\mu\text{mol Se/kg}$  $\text{HBV}_{\text{Se}}$ 

(6 graphs comparing Se Deficit or surplus of different seafoods)

Fig. 3. The relative Se deficit or excess ( $\mu\text{mol}/\text{kg}$ ) shown in relation to seafood Hg contents.

# Se Deficit or Surplus



**Table 1.** Seafood Mercury Contents and Relationships to Body Weight

Seafood	n	Body Wt.	mg Hg/kg	$\mu\text{mol Hg/kg}$	Slope (Hg x Wt.)	Adj. R <sup>2</sup>	F	p value
Pilot whale	18	992.4 $\pm$ 507.6	1.56 $\pm$ 0.73	7.75 $\pm$ 3.62	0.004(x) + 3.51	0.32	8.93	<0.01
Mako shark	10	57.4 $\pm$ 12.5	1.81 $\pm$ 0.40	9.01 $\pm$ 1.99	0.111(x) + 2.66	0.41	7.41	0.03
Swordfish	49	80.8 $\pm$ 55.8	1.00 $\pm$ 0.37	4.99 $\pm$ 1.85	0.017(x) + 3.91	0.09	6.16	0.01
Thresher shark	10	71.3 $\pm$ 69.4	0.97 $\pm$ 0.32	4.86 $\pm$ 1.60	0.032(x) + 2.57	0.26	4.24	0.07
Bigeye tuna	50	41.2 $\pm$ 20.4	0.60 $\pm$ 0.25	3.00 $\pm$ 1.23	0.040(x) + 1.34	0.44	39.02	< 0.001
Skipjack tuna	10	8.6 $\pm$ 1.2	0.34 $\pm$ 0.10	1.67 $\pm$ 0.52	NS	NS	NS	NS

**Table 2.** Seafood Selenium Contents, Selenium Deficit or Surplus, and Health Benefit Values.

Seafood	n	mg Se/kg	$\mu\text{mol Se/kg}$	$(\mu\text{mol Se-Hg/kg})$	HBV
Pilot whale	18	0.41 $\pm$ 0.31	5.23 $\pm$ 3.88	-2.52 $\pm$ 6.40	-14.79 $\pm$ 19.98
Mako shark	10	0.32 $\pm$ 0.04	4.07 $\pm$ 0.48	-4.93 $\pm$ 1.79	-16.44 $\pm$ 8.57
Swordfish	49	0.43 $\pm$ 0.12	5.40 $\pm$ 1.48	0.41 $\pm$ 1.80	0.28 $\pm$ 3.73
Thresher shark	10	0.52 $\pm$ 0.12	6.55 $\pm$ 1.51	1.68 $\pm$ 1.43	2.67 $\pm$ 2.04
Bigeye tuna	50	0.99 $\pm$ 0.28	12.38 $\pm$ 3.47	9.40 $\pm$ 3.73	11.47 $\pm$ 3.79
Skipjack tuna	10	1.56 $\pm$ 0.92	19.83 $\pm$ 11.71	18.15 $\pm$ 11.74	19.61 $\pm$ 11.83