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The Honorable Patrick J. Leahy
United States Senate
Washington, D.C. 20510-4502

Dear Senator Leahy:

Thank for your letter of October 7, 1999, addressed to Secretary Donna E. Shalala, co-signed by Senator Thomas Harkin, regarding the Food and Drug Administration's (FDA or the Agency) policies on methylmercury in seafood. The Secretary has asked FDA to respond to you. This is an important issue to FDA, and we welcome the opportunity to discuss it.

As you are aware, humans are primarily exposed to methylmercury by consuming fish. This is because methylmercury accumulates through the aquatic food chain to fish in fresh water and marine environments, with the highest levels found in large predator fish such as shark and swordfish. The result is that nearly all fish contain trace amounts of methylmercury. In most marine fish, methylmercury levels range from less than 0.01 parts per million (ppm) to 0.5 ppm. However, in a few species of fish, most frequently the larger, long-lived predator fish, the levels can be 1 ppm and higher. Canned tuna, which is composed of smaller species of tuna, averages about 0.17 ppm. Overall, levels in the seafood supply average about 0.12 ppm.

As you noted in your letter, methylmercury exposure is of special concern to pregnant women, women who may become pregnant, fetuses, and the young. At high levels of exposure, methylmercury can pass through the placenta and cause adverse developmental effects and other negative health outcomes. We are not aware at this time, however, of any convincing data that suggest that FDA's action level is not adequately protective of the developing fetus. However, as a matter of prudent public health policy, FDA has issued advice to pregnant women and women of childbearing age to limit their consumption of shark and swordfish to no more than once a month.

FDA's review, however, of the level is a continuing effort. As new data become available, they are included in its consideration of the revision of the action level. Studies in the Seychelles and Faroe Islands, which have attempted to shed light on the effect of methylmercury on the developing fetus, have provided significant new information. These studies have also been subject to review at an interagency workshop and are now included in a National Academy of Science (NAS) panel review. FDA is following the progress of the NAS review, as well as follow-on work in the Faroes and Seychelles. This NAS study, as mandated in an Environmental Protection Agency (EPA) budget authorization, is an evaluation of research findings relevant to EPA's methylmercury reference dose (RfD) for protecting human health. The mandate does not include FDA's action level. However, we look forward to the publication of the results of the NAS study and will consider them in our reviews. A determination of the need to revise the action level for methylmercury will include a process for public comment.

The following is the Agency's response to your specific questions:

1. Action Level

> a. As we understand it, the original action level established by FDA for mercury in 1969 was 0.5 ppm, or twice as stringent as the current standard. On what scientific or other basis was the current action level of 1.0 ppm established? That is, was it set at a level that would be protective of the health of sensitive populations (e.g. women of childbearing age, pregnant women and their fetuses, and young children) with a margin of safety? Or, was it set at a level that is only protective of adult humans?

Action levels announce the amount of a particular added contaminant that FDA may regard as resulting in adulteration under section 402(a)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 342(a)(1)). That section provides that a food is adulterated if it bears or contains an added poisonous or deleterious substance that "may render [the food] injurious to health." Please note that action levels are not binding on the Agency, the courts, or the regulated industry.

The current action level for methylmercury reflects a consideration of the hazards of methylmercury and the result of a data-based exposure assessment involving numerous approaches to establishing contamination levels, consumption patterns, and exposure measurements. FDA's action level of one ppm for methylmercury in fish was established to limit consumers' methylmercury exposure to levels more than ten times lower than the lowest levels associated with adverse effects (paresthesia) observed in poisoning incidents. FDA based its action level on the lowest level at which adverse effects were found to occur in adults. In fact, dietary exposure for adults is lower than the lowest level found to affect fetuses, and thus, that adult exposure level will still afford the fetus protection.

b. Does the action level incorporate or otherwise reflect economic considerations? Specifically, is the action level as a matter of law or practice set at a less protective level than if it were based solely on protection of human health and, if so, is that less protective level selected due to economic, cost or other non-health-related considerations? What was the role, if any, of the fishing industry in setting the 1 ppm level?

The action level set by FDA does not incorporate or otherwise reflect economic considerations. The level is based on protection of human health, taking into account potential exposure levels. The fishing industry played no direct role in establishing the action level. The industry was involved in the consideration of the action level before it was finalized in 1979 (Volume 44 Federal Register page 3990; January 19, 1979) only through the submission of comments and through litigation in Federal court. (See U.S. v. Anderson Seafoods, Inc., 447 F. Supp. 1151 (N.D.Fl. 1978); aff'd, 622 F.2d 157 [5th Cir. 1980]).

c. Does the current action level reflect trends in per capita consumption of fish, especially in women of childbearing age, pregnant women and young children since that level was established in 1979? Does information collected by FDA on consumption suggest that there has been an increase in mercury exposure to the American public, and especially to Native Americans, subsistence fishers and sensitive populations? If so, has FDA found that there has been a corresponding increase in mercury body burden for these

sub-populations? Please discuss why, given an increase in mercury exposure, FDA would or would not expect a corresponding increase in human health risk for these sub-populations.

To best address methylmercury exposure using dietary models, detailed information is needed to address long-term patterns of how often and in what amounts people of different population sub-groups eat particular fish species. Unfortunately, there is no current nationally representative food consumption survey data that provide such information. Accordingly, in our exposure assessment, consumption data from a number of sources were considered. The National Marine Fisheries Service (NMFS) 1978 study, "Report on the Chance of U.S. Consumers Exceeding the Current Acceptable Daily Intake for Mercury and Recommended Controls," is still considered the most complete picture of long-term dietary patterns of methylmercury exposure from fishery products. However, we recognized that the NMFS analysis was performed over twenty years ago and fish consumption patterns may have changed somewhat since then. Dietary preferences may change and the availability of fish, especially larger species, may decrease as global fisheries are depleted. In order to incorporate these changes into our calculations, a number of other dietary surveys were considered.

One approach involves a simple population based per capita exposure analysis using 1995 per capita consumption data from NMFS. Another approach for characterizing methylmercury exposure over extended periods uses recall data from the National Health and Nutrition Examination Survey III (NHANES III). In this survey, adult participants were questioned about the number of seafood meals they ate the previous month. This information was collected by the Centers for Disease Control and Prevention (CDC) from 1988 to 1994. However, recall data for children participants were not collected.

Other sources of consumption data included in the FDA exposure assessments are the 14-Day Menu Census (1982-87) conducted by the Market Research Corporation of America, the 1977-78 U.S. Department of Agriculture (USDA) National Food Consumption Survey (NFCS), and the combined three-day USDA Continuing Survey of Food Intake by Individuals (CSFII) for 1989-1992.

FDA is continuously evaluating its exposure assessments. Overall analysis of these dietary surveys does not indicate significant changes in fish consumption and therefore in methylmercury exposure levels either in the general population or specific subpopulations. Therefore, based upon current information, we have no reason to believe that there has been a corresponding increase in methylmercury body burdens.

The data used in FDA's exposure assessments was not of sufficient specificity to make recommendations for subpopulations such as Native Americans and subsistence fishers. Additionally, FDA has jurisdiction over fish products involved in interstate commerce, so that small scale fishing that is local or occurs within a State by sport/recreational or subsistence fishers or by Native Americans would not be in FDA's purview. Risks to these populations are normally addressed by regional health authorities (*e.g.*, State departments of health) through fish advisories and enforcement activities.

d. Has the FDA developed guidance for all Americans on how often and how much certain kinds of contaminated fish can be safely consumed? If so, do these publications explicitly state who the action level was (or was not) established to protect? Further, explain how FDA's guidance takes into account variations within the general population and sub-populations, including differences in weight, consumption patterns, and the ability to eliminate mercury from the body.

In September 1994, FDA seafood specialists stated in a published advisory in the *FDA Consumer* magazine article (see enclosure 1) that eating a variety of types of fish, which is the normal pattern of consumption, does not put anyone in danger of methylmercury poisoning. However, FDA specifically advised pregnant women and women of childbearing age who may become pregnant to limit their consumption of shark and swordfish (which have the highest levels of methylmercury) to no more than once a month. For the general population, regular consumption of fish species with methylmercury levels around one ppm - such as shark and swordfish - should be limited to about seven ounces per week (about one serving) to stay below the acceptable daily intake for methylmercury. For those fish species with levels averaging between 0.5 and one ppm, regular consumption should be limited to about

14 ounces per week. Current evidence indicates that nursing women who follow this advice do not expose their infants to increased risk from methylmercury.

2. Monitoring

a. Certain foods are known to contain high levels of mercury. These often include larger predatory fish such as tuna, shark, swordfish, sea bass, halibut, Spanish mackerel, king mackerel, and marlin. Does FDA itself monitor these and other fish for mercury levels, whether sold fresh, frozen or canned, and does it also work in conjunction with other federal and state agencies to do so? If so, which agencies does FDA work cooperatively with and to what extent?

FDA monitors a wide variety of both domestically caught and imported fish for methylmercury levels, in the fresh, frozen, and canned states. FDA has issued two methylmercury import alerts: one for swordfish (April 6, 1990) and one for fresh or frozen shark (October 25, 1991). These import alerts are guidance to FDA's field force and to industry on the level of methylmercury in these fish that FDA may consider to be adulterated under the Federal Food, Drug, and Comestic Act. Import alerts identify problem commodities and/or shippers.

Over the period of 1992 through 1998, nine types of fish were tested in domestic compliance programs, 27 for domestic surveillance programs, 17 for import compliance programs, and 20 for import surveillance programs. A total of 37 types of fish were analyzed for methylmercury: barracuda, bass (freshwater), bluefish, bonito, carp, catfish (freshwater), cod, croaker, eels, flounder, gar, grouper, haddock, hake, halibut, mackerel (including Spanish mackerel), mahi mahi, marlin, milkfish, ocean perch, orange roughy, pike, pollock, salmon, sea bass, sea trout, shark, smelt, snapper, sole, suckers, swordfish, tilapia, trout, tuna, whitefish, and whiting.

In addition, FDA's annual market basket survey, the Total Diet Study (TDS), analyzes a total of 47 foods for total mercury, seven of which are seafood products. These items are tuna, canned in oil; frozen, heated fish sticks; pan-cooked haddock;

boiled shrimp; homemade tuna noodle casserole; fast-food fish sandwich on bun; and canned New England clam chowder. FDA works with officials from other Federal and State agencies whenever possible. Personnel in FDA field offices interact with their counterparts in most states to carry out additional contaminant monitoring. The extent of these cooperative efforts varies among the States and depends on the size and scope of the program in the individual States. FDA also acquires and uses state-generated data to complement its own and other federally sponsored programs. It also relies upon cooperation with the U.S. Customs Service in the monitoring of fish imports and with the EPA for monitoring of environmental contamination events.

b. For each of the past ten years (1988 through 1998), describe FDA's monitoring program for chemical contaminants (specifically mercury) in fish. More specifically, provide detailed information on the following: the number of areas monitored for mercury in fish; the location of these areas; the testing frequency for fish in these areas, the species, age, size and sex of the fish tested, the method of testing (including quality assurance and quality control/chain of custody issues); and the type of sample used in testing (i.e. fillet, steak or whole fish). Also, for the same time period, provide information, including data, on both the number and the percentage of samples for each species which tested over FDA's action level. Were fish caught from that area withdrawn from sale to market(s)? How much of these fish caught were withdrawn (as percent of total yearly catch and weight for that species)? Has the FDA banned sale of fish from specific waters and how does FDA ensure that fish caught from these waters are not sold in domestic markets? What is done with fish banned from sale by FDA?

FDA monitors food in interstate commerce. It does not monitor specific geographic areas. However, we believe there is no demonstrated need to monitor geographic aquatic areas for methylmercury levels in commercial species of fish. Methylmercury levels in commercial fish are known to fall within certain ranges primarily on the basis of species rather than geographic area. Moreover, those ranges have proven to be quite stable over time. In the absence of some highly unusual

event, such as an industrial discharge like the one that occurred in Japan many years ago, FDA has no reason to expect levels in commercial species to change significantly. Should FDA learn of a discharge event, through the EPA or other means, we would then focus our monitoring efforts on that event.

The summary data of fish and fish product methylmercury monitoring was obtained from two FDA databases. Enclosure 2 covers the period of 1988 through 1991 and Enclosure 3 covers 1992-1998. Enclosure 3 is comprised of retail samples from 35 States or territories from compliance or surveillance efforts. These States and territories are: Alabama, Alaska, Arkansas, California, Colorado, Florida, Georgia, Hawaii, Illinois, Kansas, Louisiana, Maryland, Massachusetts, Michigan, Minnesota, Mississippi, Missouri, Nebraska, Nevada, New Jersey, New York, North Carolina, Ohio, Oregon, Pennsylvania, Puerto Rico, Rhode Island, South Carolina, Tennessee, Texas, Virginia, Washington, West Virginia, Wisconsin, and Wyoming.

Enclosure 2 also consists of retail compliance and surveillance import and domestic samples, but this data is not easily available with detail on import or domestic status or State where collected. Enclosure 2 consists of 577 samples analyzed over four years. In 1988, 58 samples were analyzed; in 1989, 62 samples were analyzed; in 1990, 11 samples were analyzed; and in 1991, 446 samples were analyzed. Enclosure 3 consists of a total of 1479 samples that were analyzed over this seven-year period and includes information about the import status of the samples. In 1992, 240 domestic samples and 183 import samples were analyzed; in 1993, 144 domestic and 156 import; in 1994, 141 domestic and 115 import; in 1995, 33 domestic and 124 import; in 1996; 33 domestic and 134 import; in 1997, 56 domestic and 93 import; and in 1998, no domestic and 27 import samples were analyzed.

Total mercury is determined by using a nitric/sulfuric acid mineralization procedure with quantification by cold vapor atomic absorption spectrometry. Limits of detection and limits of quantification were defined to be, respectively, three and ten times the standard deviation of replicate measurements of independent control blanks. These limits depended in part on the amount of food analyzed and the dilution amounts specified by the method. The nominal limits for methylmercury, based on

a 5 g test portion, may be as low as 0.006 mg/kg (detection) and 0.02 mg/kg (quantification).

The form of food samples tested by FDA generally corresponds to whatever form would ordinarily be consumed. This is typically a fish fillet. In FDA's Total Diet Study (TDS), it may be a prepared food item or an ingredient. Since samples of fish are generally in the fillet form or further processed, the biological species, size, age, and sex of the fish from which they were taken are not determinable.

Data regarding violative results of compliance and surveillance monitoring are provided in Enclosures 2 and 3. From mid-1993 to early 1997, no samples from the TDS were found to be violative. Earlier TDS results, as generally described in the attached reprint "FDA Total Diet Study, July 1986-April 1991, Dietary Intakes of Pesticides, Selected Elements, and Other Chemicals" (Enclosure 4), also do not indicate high levels of mercury in seafood.

It is not possible at this time given currently available data to quantify the proportion of fish and fish products annually withdrawn from retail sale.

As stated earlier, FDA regulates foods, and, thus it does not regulate fishing itself in inland or coastal waters. This responsibility falls to local and State governmental bodies and the Department of Commerce. FDA's statutory mandate with regard to methylmercury in fish and shellfish extends to commercial species in interstate commerce. FDA can, however, issue advisories if it feels an ongoing contamination problem exists that may compromise the health and safety of consumers. These advisories serve as notice to State and local jurisdictions to investigate possible hazards and take appropriate action.

Domestically caught fish from a lot that is determined to be adulterated due to methylmercury levels, and that can be located and recovered, is removed from retail and destroyed.

Lots of fish and fish products intended for import that appear to be adulterated because of the level of methylmercury contained therein may be denied entry into the U.S. and released to the importer. The importer may destroy the

shipment, export to another destination, or submit a reconditioning proposal that would eliminate the violation. While the latter is a theoretical possibility, FDA is unaware of an instance where reconditioning of the methylmercury-contaminated fish has occurred.

c. Does FDA's monitoring program include all domestically sold fish (including imported canned, fresh, frozen and dried fish)? If so, please describe these monitoring efforts. What measures does FDA take to ensure the safety from chemical contaminants (specifically mercury) of fish processed outside the United States that is sold domestically? If domestic catch or imported fish from foreign producers are not included in monitoring programs, what assurances do American consumers have that these fish are safe to eat?

FDA samples individual lots of domestically produced and imported fish and fish products and analyzes them for contaminants to evaluate whether they are adulterated within the meaning of the FD&C Act (Section 402(a)(1)). Domestic samples are collected as close as possible to the point of production in the distribution system; import samples are collected at the point of entry into U.S. commerce. Emphasis is on the raw, whole commodity; however, processed foods such as dried or frozen fish are also sometimes included. If contaminants are found in domestic samples, FDA can invoke various sanctions, such as seizure or injunction. For imports, shipments may be stopped at the port of entry when contaminants are found.

When collected, domestic and imported food samples are classified as either surveillance or compliance. Most samples collected by FDA are the surveillance type; that is, there is no prior knowledge or evidence that a specific food shipment contains contaminants. Compliance samples are taken as follow-up to the finding of a contaminant or when other evidence indicates that a contamination problem may exist. Factors considered by FDA in planning the types and numbers of samples to collect include review of recently generated State and FDA contaminant data, regional intelligence on contamination, and information on the amount of domestic and imported food that enters interstate commerce.

FDA regulates fish in interstate commerce. Locally caught fish in any form is therefore not monitored by FDA.

d. Has there been a discernible trend in the body burdens of mercury in fish or in human consumers? If body burden trend data are available, please provide detailed information by population subgroup, including Native Americans, subsistence fishers and other vulnerable sub-populations such as pregnant women, women of childbearing age, infants and young children.

FDA has not detected, based on currently available data, a significant trend in the methylmercury body burdens of fish or of human consumers. Methylmercury levels found in fish are consistent with observations from the early 1970s, when the presence of methylmercury was first determined. Long-term fish consumption is a major determinant of methylmercury blood and hair concentrations. The concentrations of methylmercury in hair are proportional to the blood concentrations at the time of formation of the hair strand. Once methylmercury is incorporated into the hair strand, its concentration remains unchanged and serves as an excellent biomarker by which methylmercury exposure can be recapitulated over a period of time. Comparisons of hair biomarker results from available studies, involving both children and adults, with some studies focused on women of childbearing age and pregnant women, do not indicate significant increases in the body burden of U.S. consumers.

There is human body burden evidence of exposure to methylmercury in studies from the 1970s, 1980s, and 1990s. Although these studies represent different time periods, they also represent different population groups and geographic regions. Collectively, however, they do not allow for any meaningful analysis of trends in human exposure for methylmercury body burdens. Although these data do not allow for a trend analysis, they do support the exposure conclusions used by FDA to establish its action level.

3. General Information

a. Information on the nutritional value and contents of most packaged foods is disclosed on the labels of those foods. Increasingly, many fresh meats also contain comparable

information, including food safety warnings to cook meat and poultry thoroughly where there is a risk of food borne illness. In contrast, fresh seafood is not accompanied by similar information despite consumption of uncooked seafood being associated with a risk of food-borne illness (for example, raw shellfish) and the fact that there are fish consumption advisories for mercury in most of our country. Instead, the FDA utilizes other information in its risk communication efforts. Please provide samples of leaflets and other forms of consumer publications regarding consumption of mercury-contaminated fish and explain how FDA reaches out to culturally distinct sub-populations. For each leaflet or publication, please state how many copies were printed and when, as well as how they were disseminated, to whom and in what quantities. Please provide specific examples of FDA's efforts to convey this information to sensitive populations, for example, by providing literature to pediatricians, obstetricians, and gynecologists. If such efforts to disseminate information have not occurred, please explain why not.

Regarding consumer publications on consumption of fish containing mercury, please see Enclosure 1, "Mercury In Fish: Cause For Concern?" a reprint from the *FDA Consumer* magazine. It was originally published in September 1994, and extracted and reprinted in May 1995. *FDA Consumer* magazine had a total circulation of 28,500 per issue in 1994, primarily mailed to paid subscribers who consist of a wide range of people with an interest in public health issues.

Fifty thousand copies of the reprint were printed in 1995, and most of these have been distributed. 5,200 copies were sent to public affairs specialists around the country for public outreach; 1,378 were sent to the Government Printing Office for distribution to institutions such as libraries; 1,410 were distributed to FDA Headquarters in Washington, D.C., for immediate response to consumer inquiries, and 42,012 were warehoused to be distributed as needed. Of the warehoused copies, few remain.

FDA also relies upon its Internet website for consumer education and outreach. The aforementioned reprint is also posted on the Center for Food Safety and Applied Nutrition

(CFSAN) website (URL: www.cfsan.fda.gov), along with other consumer and producer information. These can be accessed through a variety of links (Seafood; Consumer Advice; Imports, Exports, Inspections, Recalls; Pesticides and Chemical Contaminants; and Women's Health), as well as through the Question and Answer module, and by searching the website using keywords. The susceptible subpopulations identified by FDA, pregnant women and women of childbearing age, have been a special target of these internet outreach efforts. The CFSAN website registered 2,175 hits on the methylmercury-linked pages in October 1999 alone.

We thank you for your interest and hope you find that this information meets your needs. The Agency would be happy to meet with and provide additional information for you or your staff, should you desire it. A similar letter has been sent to your co-signer.

Sincerely,

Melinda K. Plaisier
Associate Commissioner
for Legislation

4 Enclosures
"*FDA Consumer* - Mercury In Fish"
"Table 1 - FDA Methyl Mercury Analytical Results in Fish, Domestic and Imported, 1988 - 1991"
"FDA Methyl Mercury Analytical Results in Fish, Domestic and Imported, 1992 - 1998"
"FDA Total Diet Study, July 1986-April 1991, Dietary Intakes of Pesticides, selected Elements, and Other Chemicals" - Gunderson: Jounal of AOAC International