OFFICE OF THE COMMISSIONER MEETING
EXECUTIVE SUMMARY

Date: November 14, 2000
Time: 9:30 - 10:30 a.m.
Location: Commissioner's Conference Room, 14-68 Pkln.

Subject: Methylmercury in Fish

Attendees: Jane Henney; Sharon Holston; Bill Hubbard, Mel Plaisier; John Marzilli, Debbie Ralston, John Taylor; Margaret Porter/Leslie Kux; Joe Levitt, Bob Buchanan, Mike Bolger, Bob Lake, Alan Levy, Marjorie Davidson, Phil Spiller, Lou Carson, Ms. Tamar Nordenberg (CFSAN)

Purpose: To brief the Commissioner about the National Academy of Sciences' report (issued in July) on the toxicological effects of methylmercury and CFSAN's recommendations on revising its advisory about consumption of fish with higher levels of methylmercury

Issue: EPA's FY 1999 appropriations bill directed EPA to contract with NAS to examine the validity of EPA's reference-dose (RfD) for methylmercury. NAS concluded that EPA's RfD is a scientifically justifiable level to protect public health. Both the report (p. 325) and the NAS press release noted (but did not document) that an estimated 60,000 U.S. children may be at risk of neurological problems because of prenatal exposure to methylmercury. Consumer advocates, the industry, and Congress are aware that CFSAN will decide about revising its current advisory as early as November 20. The draft conference report to the FY 01 Labor-HHS Appropriations (on which FDA commented) directed the DHHS not to revise the advisory "without highly credible science" (including final data from the Seychelles study) and in consideration of the health benefits of fish consumption. The draft language directed the Secretary to report back to the appropriations committees no later than November 30, 2000. Also, a WHO committee found data from two studies inconclusive and recommended waiting for new data in 2002. One should also note that FDA said in an interim response to a 1992 CSPI petition for a stricter methylmercury standard that we would have more information from the Seychelles study. (See **TAB A** for more detail on NAS report, WHO evaluation, stakeholder input, focus group test of a consumer advisory, committee report language.)

Agenda:

Joe Levitt	Introduction	5 minutes
Mike Bolger	NAS & WHO reports & study data	10 minutes
Alan Levy	Focus group information	10 minutes
Phil Spiller	Impact of advisory on regulation	10 minutes
Lou Carson	Stakeholder meetings: feedback	10 minutes
Joe Levitt	Summary and recommendations	5 minutes
	Discussion/questions	10 minutes

Background: Human exposure to methylmercury (MeHg), one organic form of mercury, results primarily from fish consumption. MeHg accumulates in marine and freshwater fish through the food chain. Nearly all fish contain at least trace amounts; in most marine fish, levels range from less than *0.01 parts per million (ppm) to 0.5 ppm*. The highest levels are found in larger, long-lived marine fish species (e.g., shark, swordfish, tuna), which can contain *1 ppm levels or higher*. High levels are also found in some freshwater species (bass, pike, and walleye).

Source - About half of environmental mercury occurs from vapor escaping from the earth's core. Most of the rest comes from smokestack emissions, which EPA regulates under the Clean Air Act.

Health Concerns - High levels of methylmercury exposure from accidental poisoning incidents have caused adverse developmental effects and other negative health outcomes. The fetus is more sensitive to MeHg's toxic effects. One study (Faroe Islands) showed an association between chronic, low-dose prenatal exposure and poor results on neurobehavioral tests in their children. However, the study population was also exposed to persistent organic pollutants reported to have similar neurotoxic effects, confounding the interpretation of the study's results.

Health Benefits from Eating Fish - Fish are cited as a good source of protein, omega-3 fatty acids and other lipids, and other nutrients that help infant brains to develop and may protect against heart disease. The American Heart Association recommended this year, for the first time, that people eat two servings of fatty fish such as tuna or salmon a week.

FDA's Action Level - *One part per million* is FDA's action level, based in part on a tolerable daily intake of about 0.4 grams per kilogram of body weight per day. This level represents a 10-fold margin of safety from the levels at which adverse effects are observed in adults.

Levels of Fish Consumption - FDA's analysis of various dietary surveys since a comprehensive report in 1978 does not point to significant changes in fish consumption, or, in turn, methylmercury exposure in the general population or specific subpopulations, such as women of childbearing age.

FDA's Consumer Advisory - FDA seafood experts stated in an advisory published in a September 1994 *FDA Consumer* article that eating a variety of types of fish, the normal pattern of consumption, does not put anyone in danger of methylmercury poisoning. The agency advised pregnant women and those who may become pregnant to not eat shark and swordfish more than once a month. The general population should not eat more than about 7 ounces a week of fish species with high methylmercury levels, and not eat more than about 14 ounces a week of species with medium levels (*0.5 to 1 ppm*). However, the advisory said that Americans did not need advice about the 10 most-consumed seafood species (about 80% of the market): canned tuna, shrimp, pollack, salmon, cod, catfish, clams, flatfish, crabs, and scallops. Levels are low in the smaller tuna species used for canning and in the other species listed (*less than 0.2 ppm*). (See **TAB B** for more on these topics.)

Consumer Focus Group Testing - FDA conducted eight focus groups in October to test mercury messages prepared by four groups. FDA's experts concluded that none of the four messages succeeded in communicating the risks from mercury in fish or the behaviors that could reduce such risk. People in the focus groups tended to conclude that if pregnant women were at risk of consuming too much mercury, then so were members of the general public. Also, people tended to identify different fish species as "safe" or "not safe," without absorbing the advice about the amount of fish consumption.

At **TAB C** is a list of recent meetings with stakeholders about methylmercury levels in fish.

Attachments

TAB A – Detailed information on current status
TAB B – Detailed background
TAB C – Meetings with stakeholders

TAB A - METHYLMERCURY: CURRENT STATUS

Nature of Current Issue

Following a National Academy of Sciences (NAS) study that examined the validity of the science used by EPA to derive its reference-dose for methylmercury, FDA is considering whether the agency should issue a revised consumer guidance on methylmercury, and if so, what the substance of the advisory should be.

NAS Report: *Toxicological Effects of Methylmercury*, National Research Council, released July 2000

EPA's FY 1999 appropriations bill directed the EPA to contract with NRC to provide recommendations on the derivation of a scientifically appropriate reference dose for methylmercury. NRC looked at toxicological, epidemiological, and exposure data from food and water to make determinations about the appropriate study, end points of toxicity, and uncertainty factors EPA used.

The NAS concluded that EPA's RfD of 0.1 μ/kg per day is a scientifically justifiable level for the protection of public health, but recommended that the Iraqi study on which EPA based its RfD no longer be used as the scientific basis.

Studies Evaluated

The committee focused its evaluation on epidemiological studies on brain development following long-term exposure to MeHg, done in the Republic of Seychelles, the Faroe Islands, and New Zealand.

- "Seychelles Study" in the Republic of the Seychelles (located in the Indian Ocean off the coast of East Africa): No adverse effects attributable to MeHg were seen in the 711 children through the 66-month developmental milestone. Maternal hair samples collected at children's birth contained Hg concentrations from 0.5 to 27 ppm (mean of 6.8 ppm).

- "Faroes Study" in the Faroe Islands (part of Denmark, located in the North Sea between Scotland and Iceland): The investigators found that children whose prenatal exposures were similar to those in Seychelles had subtle developmental deficits apparent at 7 years of age. Abnormalities were seen in tests of memory, attention, and language, and to a lesser extent in neurophysiological end points. Questions have been raised regarding the population's intake of persistent organic pollutants (POP) and also the confounding role of PCBs.

Why the discrepant findings in Seychelles and Faroes? An expert panel published a report in 1999 suggesting possible explanations: differences in sources of exposures or exposure measures (fish versus marine mammals), differences in the frequency and extent of exposure (high/short-term exposures in Faroes versus lower level/chronic exposures in Seychelles), differences in the neurobehavioral tests used and the ages of the children studied, influences of confounders and covariates, and biostatistical issues involved in the data analysis.

Further Seychelles data expected soon will facilitate comparison of Seychelles and Faroe Islands data.

- New Zealand Study: Children at 4 and 6 years of age who had been exposed in utero to MeHg were tested and decrements were reported in test performance at both ages in the children exposed prenatally to moderate to high doses.

Faroes Study Selected, Seychelles Excluded

The committee selected the Faroe Islands study as the "most appropriate" study for deriving an RfD, citing advantages of the study such as: it used both hair and umbilical cord blood as measures of exposure, included a larger study population, etc.

The NAS excluded the Seychelles study data in deriving an RfD, stating that "because there is a large body of scientific evidence showing adverse neurodevelopmental effects ... an RfD should not be derived from a study, such as the Seychelles study, that did not observe any associations with MeHg."

The reason for NAS excluding Seychelles was not related to any shortcomings in the studies. In fact, the academy concluded that "there do not appear to be any serious flaws in the design and conduct of the Seychelles, Faroe Islands, and New Zealand studies that would preclude their use in a risk assessment."

NAS Statement "60,000 newborns annually might be at risk"

The NAS committee states on p. 325 of its report:

> To further characterize the risks of MeHg, the committee developed an estimate of the number of children born annually to women most likely to be highly exposed through high fish consumption (highest 5% estimated to consume 100 g per day). Available consumption data and current population and fertility rates indicate that over 60,000 newborns annually might be at risk for adverse neurodevelopmental effects from in utero exposure to MeHg.

The 60,000 number is again mentioned in NAS's press release: "[T]he committee estimated that each year about 60,000 children may be born in the United States with neurological problems that could lead to poor school performance because of exposure to methylmercury in utero."

The NAS report does not document or elaborate on its scientific basis for the 60,000 figure, leaving open the question of what scientific methods were used to arrive at this number.

Questions have been posed, too, about the NAS's use of the term "at risk," undefined in the report.

World Health Organization (WHO) Evaluation of Faroe Island and Seychelles data.

The Joint Expert Committee on Food Additives of WHO looked at the Faroe Islands and Seychelles data and found that they did not provide consistent evidence of neurodevelopmental effects in children of mothers whose intake of methylmercury came from fish and/or marine mammals. The Committee concluded that it could not evaluate the risks associated with lower intakes, and recommended that MeHg be evaluated again in 2002 when other data, including the Seychelles cohort, could be considered.

The study, published earlier this year, was not taken into consideration by the NAS committee.

FDA Stakeholder Input

- Fish Industry

In an Oct. 23, 2000, letter to Commissioner Henney (copies to Donna Shalala, Carol Browner, Dan Glickman, Norman Mineta, John Spotila, Francis Sharples, Joe Levitt), the National Food Processors

Association (NFPI) and National Fisheries Institute (NFI) requested information on how FDA would reach a scientific consensus on the issue. The organizations emphasized the impact that the MeHg decision would have on Americans' dietary habits. They said that the Faroe Islands study "bears no relationship to consumption patterns of fish consumers in the United States" and that questions exist about the methods used and the confounding intake by the population studied of PCBs and persistent organic pollutants (POPs). They urged FDA to await the Seychelles data still to come and to wait at least seven to eight months before announcing any decision on a consumer advisory.

- Letters from Congress: HHS recently has received several letters from members of Congress on the methylmercury issue.

1. In a Sept. 18, 2000, letter to Secretary Shalala, Senator Patty Murray urged FDA to consider all scientific data in assessing the MeHg issue, including the upcoming Seychelles data and the NHANES IV Consumption Study, in light of the "major impact on the choices of fish available to consumers and the ability of the seafood industry to supply fish for the commercial marketplace."

2. In a Sept. 15, 2000, letter to Secretary Shalala, five Senators urged FDA to consider all data, including that from the Seychelles and NHANES IV Consumption studies. The Senators noted that NAS did not use the Seychelles data in establishing a reference dose despite finding no serious flaws in the study's design or conduct. Like Senator Murray, they emphasized the importance of consuming a healthful diet, including protein from sources such as fish.

3. An August 15, 2000, letter to Secretary Shalala from Senators Leahy and Harkin urged FDA (and ATSDR) to abandon its current "outdated" action label in favor of the EPA's stricter standard in the interest of protecting public health. The letter added that FDA should resume its suspended tests for methylmercury contamination in domestically-caught fish.

   The letter from Senators Leahy and Harkin followed FDA's February 2000 response to methylmercury-related questions posed by the Senators in an October 1999 letter.

- Consumer Focus Group Testing

FDA conducted eight focus groups in October 2000 (half in Calverton, Md., and half in Denver) to test mercury messages prepared by each of four groups: the National Marine Fisheries Service (NMFS), EPA, FDA, and the State of Maine. The following types of groups were tested at each site:

- one group of pregnant women
- one group of men and women with at least a college degree
- one group of men and women with less than a college-degree level education
- one group of men and women regardless of education level.

FDA's experts concluded that none of the messages satisfactorily communicated the risks from mercury in fish or the behaviors that could reduce such risk. People in the focus groups tended to conclude that if pregnant women were at risk of consuming too much mercury, then so were members of the general public. Also, people tended to identify different fish species as "safe" or "not safe," with little regard to the message's quantitative advice about fish consumption.

- Health advocacy groups: CFSAN has been meeting with groups representing consumers, the fish industry, and health professionals to obtain their input and ensure a comprehensive consideration of the scientific information and expected public health impacts of any decision on MeHg.

Citizen petition: In 1992, the Center for Science in the Public Interest petitioned FDA to adopt a stricter methylmercury standard. FDA responded that the not-yet-completed Seychelles data would provide additional information on the issue.

Proposed Conference Report Language to FY 01 Labor-HHS Appropriations:

- Proposed language:

Background:
The U.S. Food and Drug Administration is considering issuance of new consumer guidance on methylmercury in fish as early as November 20, 2000. FDA has indicated its guidance will be based on a study, the Faroe Islands study, that bears no relationship to consumption patterns of U.S. fish consumers. A number of toxicologists have raised concerns about using the Faroe Islands study as the basis for consumer guidance on fish consumption in the U.S. FDA and EPA have continued to fund the Seychelles study, which is near completion and includes a direct comparison of outcomes from identical test batteries in the Faroe Islands study. The proposed language is intended to convey Congressional intent that HHS include the imminent "Seychelles study" results in its analysis of methylmercury and fish, and any related consumer advisory revisions.

Conference Report Language:
The conferees are aware that the Department of Health and Human Services is reviewing its consumer advisory on the public health effects of exposure to mercury from seafood consumption. The conferees expect the Department to revise its consumer advisory on this subject only as warranted by highly credible scientific information, particularly including imminent studies that examine potential human exposure to mercury from seafood consumption that most closely reflect U.S. dietary habits. To ensure consistency in government public health messages, any revisions in this advisory shall be consistent with U.S. dietary guidance and take into account the public health benefits of consuming seafood and seafood products. The Secretary is expected to report to the Committees on Appropriations no later than November 30, 2000 on agency actions to review such a consumer advisory.

- FDA has requested that some of the language be deleted or substantially modified to preserve the agency's autonomy to act.

Tabs

1. NAS study executive summary
2. Background document on methylmercury in fish and FDA's action level
3. Current FDA advisory
4. Three letters from Congress
5. Stakeholder meetings attendees list
6. NFPA letter
7. EPA's draft "Reference Dose for Methylmercury" document

TAB B – METHYLMERCURY: DETAILED BACKGROUND

Source - Methylmercury (MeHg), one organic form of mercury, is a neurotoxin; human exposure results primarily from fish consumption. MeHg accumulates in fish through the food chain in fresh water and marine environments. Nearly all fish contain at least trace amounts; in most marine fish, levels range from less than 0.01 parts per million (ppm) to 0.5 ppm.

The highest levels are found in larger, long-lived marine fish species (e.g., shark and swordfish), which can contain 1 ppm levels or higher. Similar levels are found in some freshwater species (e.g., bass, pike, and walleye).

Health Concerns, Health Benefits - Health risks depend largely on the exposure levels. The fetus is more sensitive to MeHg's effects, making exposure a special concern to women of childbearing age.

High levels of exposure from accidental poisoning have caused adverse developmental effects and other negative health outcomes. One study showed an association between chronic, low-dose prenatal MeHg exposure from maternal fish consumption and poor performance on neurobehavioral tests. However, this study's observations are complicated by the confounding exposure to persistent organic pollutants reported to have similar effects on neurological development.

On the benefits side, fish are cited as a good source of protein, lipids like omega-3 fatty acids, and other essential nutrients possibly protective against heart disease and beneficial in infants' brain development. The American Heart Association, in its year 2000 dietary guidelines, recommended for the first time that people eat two weekly servings of fatty fish, such as tuna or salmon.

FDA's Current Action Level and Other Agencies' Standards - FDA's action level – that is, the level at which FDA may take legal action to remove a product from the market -- is 1 ppm for methylmercury in fish. The action level is based in part on an acceptable or tolerable daily intake (ADI/TDI) of about 0.4 µg/kg/day, depending on body weight. This ADI/TDI represents a 10-fold margin of safety from levels where adverse effects (parathesia) have been observed in adults.

FDA's exposure assessment considered consumption data from a number of sources. The National Marine Fisheries Service 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, but because the study was performed more than 20 years ago and fish consumption patterns may have changed somewhat since then, a number of other dietary surveys were considered:

- simple population-based per capita exposure analysis using NMFS 1995 per capita consumption data
- CDC data from the National Health and Nutrition Examination Survey III, in which adults were asked the number of seafood meals they ate the previous month. The data, collected form 1988 to 1994, did not include recall data for children.
- 14-day Menu Census (1982 to 87) conducted by the Market Research Corp. of America
- 1977-78 USDA National Food Consumption Survey
- combined three-day USDA Continuing Survey of Food Intake by Individuals for 1989-92.

Analysis of these dietary surveys overall does not indicate significant changes in fish consumption or, in turn, methylmercury exposure and methylmercury body burdens in the general population or specific subpopulations.

The current action level of 1 ppm in 1979 replaced a previous action level of 0.5 ppm after a court in the *Anderson Seafood* case found that the preponderance of the evidence showed no reasonable certainty of harm with up to 1 ppm. A large NMFS study one year later looked at consumption data and MeHg levels in fish, revealing a lower exposure than previously thought and supporting the Anderson decision.

Historical bases for establishing safe levels of MeHg exposure (e.g., RfD, ADI, TDI) were poisoning incidents in Japan through consumption of pollution-contaminated fish and in Iraq through consumption of home-made bread that contained a mercury-based fungicide. FDA's action level was based in part on the poisoning events in Minamata Bay and Niigata, Japan, which were associated with death, permanent brain damage, and neurologic symptoms including neurodevelopmental effects in the fetuses of exposed mothers:

EPA's current RfD for methylmercury in fish is 0.1 μg/kg, determined based on data from the poisoning episodes in Iraq, although EPA recently proposed keeping the same RfD but changing the basis for the number.

ATSDR's minimal risk level of 0.3ug/kg per day is based on a dose of 1.3 μg/kg per day and on results from the Seychelles study.

FDA's Consumer Advisory.

In September 1994, FDA seafood specialists stated in an advisory published in the *FDA Consumer* magazine article that eating a variety of types of fish, which is the normal pattern of consumption, does not put anyone in danger of methylmercury poisoning.

The agency 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.

FDA advised that for the general population, consumption of fish species with these highest levels of methylmercury should be limited to about seven ounces per week (about one serving). For those fish species with levels averaging between 0.5 and 1 ppm, consumption should generally be limited to about 14 ounces per week. Evidence indicates that nursing mothers who follow this advice do not expose their infants to an increased risk from methylmercury.

Consumption advice is unnecessary for the top-10 most consumed seafood species, making up about 80 percent of the seafood market – canned tuna, shrimp, pollack, salmon, cod, catfish, clams, flatfish, crabs, and scallops. Methylmercury levels in these species are all less than 0.2 ppm, and few people eat more than the 2.2 pound suggested weekly limit of these fish.

TAB C - Meetings on Methylmercury

November 3 @ 2-4PM **NAS Study Group**

FB-8 RM 6821 Attending:

Dr Robert Goyer, Retired, Lead
Dr Joseph Jacobson, Wayne State University
Dr Michelle Catlin, NAS/NRC Study coordinator
via phone Dr Thomas Burke, Johns Hopkins University
Dr William Raub, OS, DHHS
Dr Bernard Schwetz, FDA

November 6 @ 2-4PM **National Food Processors**

FB-8 RM 6821 Attending From NFPA:*

John Cady
Rhona Applebaum
Jay Murray
Jim Coughlin
George Gray
Reps: BumbleBee; Starkist and Chicken of the Sea

*(Mr David Burney, US Tuna Foundation, cannot participate in the November 6th meeting, as he is signing an agreement and out of the country that day. He has requested either a meeting on Nov. 2 or week of Nov. 13.)

November 8 @ 10-12Noon (Rescheduled from October 24) Consumers and Women's Health Groups

FB-8 RM 6821 Attending:

Caroline Smith DeWaal, CSPI (She may invite 1-2 other consumers.)
Dr Diana Zuckerman, Patricia Lieberman, National Research and Policy for Women and Families
Carol Strobele, Children's Environmental Health Network
Cindy Pierson, National Women's Health Network
Judy Dausch, American Dietetics Assn.
Michael Bender, Methyl Mercury Project, Montpelier, VT
Susan Wood, DHHS Office of Women's Health
Kennerly Chapman, FDA OWH
Mark Silbergeld, Consumers Union

Sarah Lister, APHA
Sandra Eskin, AARP
Art Jaeger, CFA

Carol Tucker Foreman, Safe Food Coalition (not confirmed)

Additional persons expressing interest but not invited to attend as yet include:

Felice Stadler, Nat'l Wildlife Fund
Michael Green, Center for Environmental Health

Additional congressional interest that Mike Eck is following up and will invite to attend include:

Shana Friedman, Cong. Allen's (Maine)Office
Eric Juzenas , Senator Tom Harkin's (Iowa) office
Elizabeth Darrow of Senator Patrick Leahy's (Vermont) office.

And a representative from GAO that Lou Carson will invite:

Robert Pinero, GAO

TBD **USDA-WIC and FNS- awaiting call back from Julie Paradis**

TBD **Canadian Counterparts- awaiting Canada dates**

Nov 13 **NFPA Requested Meeting**

Parklawn Attending:

John Cady, NFPA
Dr. Henney
Mr. Levitt

Nov 14 **CFSAN briefing for Dr Henney: Recommendations**
Parklawn

CFSAN attendees at all meetings except the November 14 meeting will include following:

Mr. Joseph Levitt
Mr. Phil Spiller
Dr. Mike Bolger
Mr. Lou Carson
Dr. Marjorie Davidson

Dr. Alan Levy
Ms. Brenda Derby

The November 13th meeting will be limited to Dr. Henney and Mr. Levitt if Mr. Cady comes alone. If he brings other additional personnel from FDA will likely be involved.

11/3/00 (r1)