MINUTES

of the

FDA FOOD ADVISORY COMMITTEE[1]

meeting on

METHYLMERCURY

July 23-25, 2002

Sheraton College Park Hotel
Beltsville, MD

Members present: Sanford A. Miller, Ph.D., chair; Alex D.W. Acholonu, Ph.D.; H. Vas Aposhian, Ph.D.[2] Francis Frederick Busta, Ph.D.; Annette Dickinson, Ph.D.; Johanna Dwyer, Ph.D.; Lawrence J. Fischer, Ph.D.; Sarah L. Friedman, M.D. [2]; Marion H. Fuller, D.V.M.; Ms. Jean M. Halloran[2]; Joseph H. Hotchkiss, Ph.D.; Lawrence N. Kuzminski, Ph.D.; Ken Lee, Ph.D.; Margaret McBride, M.D. [2]; Thomas J. Montville, Ph.D.; Richard E. Nordgren, M.D. [2]; Robert M. Russell, M.D.; Clifford Scherer, Ph.D. [2]; Mr. Brandon Scholz; Michael W. Shannon, M.D.;

Food and Drug Administration (FDA) representatives: (Center for Food Safety and Applied Nutrition – CFSAN) Mr. Joseph Levitt; Dr. P. Michael Bolger; Dr. Robert Buchanan; Mr. Lou Carson; Dr. Margaret Cole; Dr. Marjorie Davidson; Ms. Catherine DeRoever; Ms. Linda Hayden; Ms. Carolyn Jeletic; Dr. Alan Rulis; Ms. Sylvia Smith; Mr. Philip Spiller; Ms. Natasha Williford

Guest speakers: Dr. Henry Anderson, Wisconsin Department of Health; Mr. Michael Bender, the Mercury Policy Project; Mr. Harvey Clewell, ENVIRON; Mr. Robert Collette, National Fisheries Institute; Dr. William Connor, Oregon Health & Science University; Dr. Christopher DeRosa, Agency for Toxic Substances and Disease Registry; Ms. Caroline Smith DeWaal, Center for Science in the Public Interest; Dr. Philippe Grandjean, Department of Environmental Medicine, Odense University; Dr. James T. Heimbach, ENVIRON; Ms. Jane Houlihan, Environmental Working Group; Dr. Joseph Jacobson, Department of Psychology, Wayne State University; Dr. Penny Kris-Etherton, Department of Nutrition, Penn State University; Dr. Charles Lockwood, Department of Obstetrics & Gynecology, Yale University School of Medicine; Dr. John Middaugh,

[1]Note: The entire meeting was open to the public Copies of written information provided to the Committee for consideration are available from the Committee Staff. This includes materials received from public participants. A transcript of the meeting is available from the FDA Dockets Management Branch (HFA-305), 12420 Parklawn Drive, Rockville, MD 20857.

[2]Temporary voting member

35 7200/

Alaska State Department of Epidemiology; Dr. Gary Myers, School of Medicine, University of Rochester; Dr. Susan Schober, Centers for Disease Control and Prevention; Dr. Elizabeth Southerland, Environmental Protection Agency; Mr. Richard Wiles, Environmental Working Group; Dr. Diana Zuckerman, National Center for Women and Families

Public speakers: Dr. Rhona Applebaum, executive vice president for Scientific and Regulatory Affairs for the National Food Processors Association; Dr. Fisher, dentist and private citizen; Dr. Jae Hong Lee, National Center for Policy Research for Women and Families.

Summary Conclusions

The Committee was asked to evaluate whether the agency's consumer public health advisory on methylmercury provides adequate protection for pregnant women and women of childbearing age who may become pregnant.

The Committee provided the following recommendations on ways in which the advisory could be improved:

1) better define what is meant by "eat a variety of fish" so that consumers can follow this recommendation effectively,

2) work with other federal and state agencies to bring commercial and recreational fish under the same umbrella,

3) publish a quantitative exposure assessment used to develop the advisory recommendations,

4) develop specific recommendations for canned tuna, based on a detailed analysis of what contribution canned tuna makes to overall methylmercury levels in women,

5) address children more comprehensively in the advisory to relate dietary recommendations in the advisory to the age/size of the child, and

6) increase monitoring of methylmercury to include levels in fish and the use of human biomarkers.

Agenda

The Food Advisory Committee Chair, Dr. Sanford Miller, convened the meeting at 8:30 a.m., Tuesday, July 23, 2002. Ms. Catherine DeRoever, executive secretary of the Food Advisory Committee, announced that conflict of interest reviews had revealed no potential financial conflicts for Committee members. Ms. DeRoever also reported that the guest speakers had completed financial interest forms. She informed the Committee that Dr. James Heimbach,

Mr. Harvey Clewell, Mr. Robert Collette, Dr. William Connor and Dr. Penny Kris-Etherton have financial relationships with the seafood industry.

Dr. Miller welcomed the Committee members asking them to carefully consider the questions posed by the FDA and to make recommendations based on the best available science.

Presentations—FDA (Tuesday, July 23)

Mr. Joseph Levitt, Director of the Center for Food Safety and Applied Nutrition (CFSAN), welcomed Dr. Miller and the Committee. Mr. Levitt briefly described the work leading up to the current advisory. He noted that the FDA website includes information on methylmercury levels in different fish species, as well as outreach materials on this issue.

Mr. Levitt acknowledged that the advisory is controversial and that some organizations feel the FDA fell somewhat short of the mark in the current advisory, but reiterated that the FDA genuinely believed women could protect their unborn children from methylmercury exposure based on the advice provided.

The purpose of the Committee meeting is to determine if the FDA advisory provides adequate protection for pregnant women and women of childbearing age who may become pregnant. If not, Mr. Levitt asked the Committee what changes are needed, and to give a rationale for those changes. Even if the advisory were sufficient, from a scientific standpoint, Mr. Levitt invited the Committee to recommend enhancements that would make it easier for women to follow the advice in the advisory. He provided the Committee with five questions from the FDA and asked members to listen to all views in developing its recommendations.

Presentations—FDA (Thursday, July 25)

Mr. Lou Carson presented the stakeholder outreach process that the FDA followed before it revised its advisory for methylmercury. The FDA first issued a methylmercury consumer advisory in 1994/5. In July 2000, following the National Academy of Sciences (NAS) report, the FDA decided to seek public comment on the adequacy of the 1994/5 advisory as it related to the NAS report. Stakeholders were asked six questions, from whether or not the advisory should be revised, to the data that should impact the decision to revise the advisory, to effective methods for disseminating the information. Meetings were held with various stakeholders. Feedback from the meetings and questionnaires indicated that stakeholders did not agree on when and how to proceed with a new advisory, what data should be used, and what advice should be provided to consumers. The stakeholders did agree that simple, consistent messages were needed and that diet and health are important women's issues.

In January 2001, the FDA and EPA concurrently issued methylmercury consumer advisories. In March 2001, language requested by the State of Alaska was added to the advisory, and the FDA issued a revised consumer advisory with rationale document and data tables.

Dr. Marjorie Davidson presented an overview of the focus groups consulted prior to the release of the methylmercury advisory to examine risk communication formats and gauge consumer

response to the advice. From October to November 2000, 12 focus groups were convened, comprised of mixed gender and education groups. Pregnant women were among the focus group participants. Dr. Davidson reported that the groups had little information on mercury exposure—they knew mercury was a toxic metal, but did not know about methylmercury in fish. Generally, the groups dismissed the message until they understood the message and some background information, such as why some fish had higher concentrations of methylmercury than others.

Dr. Davidson reported there was little skepticism on the factual message: Methylmercury can harm an unborn child's nervous system if eaten regularly. There was confusion however, when the groups were asked to pick a specific fish from multiple lists. Dr. Davidson reported that the groups wanted a straightforward message about which fish to eat and which to avoid. The message: "Limit consumption of certain species of fish," translated into the message: "Don't eat fish at all." The message: "You can safely eat 12 ounces of cooked fish per week," was well understood according to Dr. Davidson.

From the focus group data, Dr. Davidson noted that the most effective methods for dissemination are the media; physicians, nurses, and health departments; membership organizations; and grassroot education to populations that consume large quantities of fish. It was noted that FDA is conducting a consumer study, Summer 2002, to measure consumer trends on food safety knowledge, attitudes, and behaviors. This data will be used to analyze how effectively the advisory has influenced consumer behavior. In addition, the NHANES data from 1999-2000 will serve as a baseline and subsequent surveys will be used to determine if the advisory is having an impact.

Dr. P. Michael Bolger provided the basis for the FDA consumer advisory on methylmercury and how the advisory aligns with what is known about methylmercury. Dr. Bolger provided eight summary points:

1. Methylmercury is a neurotoxin that can have pronounced adverse effects in humans at very high doses.
2. In the United States, the consumption of fish generally is regarded as the primary exposure to methylmercury.
3. The public health questions surrounding methylmercury involve determining the exposure, over time, through fish consumption that would be necessary to cause an adverse effect.
4. In 1979, FDA developed an action level for methylmercury in fish of 1 ppm, relying primarily on data on human victims of Japanese industrial poisoning events and a study of Swedish fishermen. The action level was based on the conclusion, regarded as conservative at the time, that subtle threshold effects in adults could be associated with an amount of methylmercury in a person's hair of 5 ppm. By comparison, the hair levels of the people studied in the Faroe and Seychelles averaged about 5-7 ppm, and the average hair level of U.S. women of childbearing age is 0.2 ppm; with the 5-7 ppm level in the Faroe and Seychelles studies representing about the 99th percentile of exposure in the United States.
5. The primary purpose of the FDA's consumer advisory to pregnant women and women of childbearing age who may become pregnant is to protect the unborn child from neurologic harm from methylmercury exposure resulting from the mother's consumption of commercial fish.

6. When developing the advisory, FDA calculated that women who follow the advisory would be below "tolerable daily intake" levels, including the EPA's reference dose, which is the most conservative level of all federal agencies.
7. Baseline data indicate that 92 percent of women of childbearing age already consume below the EPA RfD.
8. The remaining 8 percent of women still have a margin of safety of about 8-fold, as compared to the RfD 10-fold factor. The goal of the advisory is to provide these women with the information they need to decrease methylmercury exposure so that their margin of safety will be at least 10-fold.

Dr. Bolger noted that the core messages in the advisory are to avoid swordfish, shark, king mackerel, and tilefish and to consume up to 12 ounces per week of all other commercial species, as long as a variety of species are consumed. The advisory also cautions individuals who eat recreationally caught fish to check for special advisories for fish caught from local waters, and that Native Americans in Alaska, who can be expected to consume well above the 12 ounces per week recommendation, should consult local authorities for fish that may be consumed more frequently.

Regarding tuna, Dr. Bolger noted that the average concentration of methylmercury in fresh or frozen tuna steaks/fillets is slightly higher than those found in canned tuna, but that these products are consumed relatively infrequently. The average concentration of methylmercury in all canned tuna is close to the average for all seafood but, he said, canned tuna is consumed in large quantities by the public. Citing data from NHANES, the Continuing Survey of Food Intake by Individuals, and other studies, Dr. Bolger reported that the data indicate that average consumption of tuna by women age 15-44 is not more than 1.7 ounces per week (less than a third of a 6-ounce can per week), and that even 95th percentile tuna eaters consume less than 5 ounces per week. These quantities compare favorably to consumption levels for the benchmark dose lower confidence limit (BMDL) of two 6-ounce cans plus a 3-ounce can per day, consumed consistently over time. The BMDL is roughly equivalent to the highest no observed adverse effect level (NOAEL) that can be calculated with confidence, or the highest dose of methylmercury that a consumer would have to ingest repeatedly in order to eventually reach a steady state body burden that is not associated with the most subtle observable effect.

Average methylmercury concentrations:

- Average level in fish: 0.12 ppm. The upper boundary of the top 10 species is 0.2. (These figures are based on FDA data collected since the 1970s and NMFS data collected in the 1970s.)
- Average levels in high-end species (fish consumers are advised not to eat): 1.0 ppm.
- Average level in mid-range species: 0.4 to 0.6 ppm (i.e., grouper, red snapper, moonfish, orange roughy, saltwater bass, freshwater trout).
- Average level in canned tuna: 0.17 ppm (0.25-0.3 in canned albacore—"white" or "solid"—tuna). The 95th percentile for canned tuna is 0.4 with albacore slightly higher.
- Average level in fresh or frozen tuna fillets/steaks: 0.35 ppm.

Dr. Bolger noted that U.S. exposure data provided by NHANES has not revealed any women of childbearing age who are exposed to levels anywhere near the BMDLs that have been derived from either the Seychelles (78 ug/day) or Faroe Islands studies (67 ug/day). He further noted that according to the U.S. consumption data, 96 percent of women who follow the advice in the FDA consumption advisory will consume less than the 12 ounces per week of a variety of seafood as addressed in the advisory. Furthermore, Dr. Bolger pointed out that these women should experience less exposure to methylmercury than the maximum contemplated in the advisory and all should consume under the RfD. Thus, they should have a margin of safety greater than 10 relative to the Faroe Islands' BMDL.

In summary, Dr. Bolger reported that methylmercury levels in the most frequently consumed species are low, including all fish in the top 10 consumed species. Because of this, the public health issue of exposure to methylmercury through commercial fish consumption involves high-end consumers out on the "tail" of the distribution curve, i.e., 96th percentile consumers or higher.

Dr. Bolger said that the FDA estimates that of the target population of women who are pregnant or may get pregnant, 92 percent already have a margin of safety/uncertainty of 10 or higher relative to the worst case BMDL, and that the remainder have an average margin of about 8. If the consumer advisory was followed, he noted, the FDA calculates that virtually the entire target population would have a margin of safety/uncertainty of 10 or higher relative to the worst case BMDL. For these reasons, Dr. Bolger noted, the FDA believes that the consumer advisory is adequate when measured against the worst-case scenario.

Guest Speaker Presentations (Tuesday, July 23)

Dr. Joseph Jacobson, National Academy of Sciences, reviewed the data on neurotoxic risks associated with exposure to methylmercury, beginning with the Japanese and Iraqi exposures, the latter of which was the first set of data used by the EPA to conduct a risk-based assessment on humans; previous assessments had been done on animals. Initially, the EPA picked an endpoint and then a cut-off level, i.e., the level at which a child does poorly, i.e., 70 on an IQ test. This is the level at which it is undesirable for an appreciable increase in the number of children performing at this level due to exposure to methylmercury. The dose response is the level of exposure that gives the desired response, with the lower limit determining the benchmark dose.

Dr. Jacobson noted that the Iraqi data, while it was the best available, was problematic because of the high exposure levels. The Seychelles and Faroe Islands studies conducted in the 1990s provided a broad range of exposures, with good overlap with U.S. exposure levels in a broad population. Dr. Jacobson noted that there were differences in the two studies.

- Seychelles measured methylmercury levels in hair; Faroe Islands measured levels in cord blood.
- The types of neuropsychological tests differed, with Seychelles being global and Faroe Islands being domain specific.
- The age at testing was different, with Seychelles testing at age 5.5 and Faroe Islands at age 7.
- The sources of exposure were different, with Seychelles women eating a variety of fish and women in the Faroe Islands eating a variety of fish as well as whale meat.

The results of the two studies, Dr. Jacobson noted, were contradictory. To explore the differences, the President's Office of Science and Technology Policy convened a workshop in Raleigh, North Carolina, that brought together four expert panels from broad areas to examine the data. The results of the Raleigh meeting were that the data from both studies were valid. No satisfactory policy findings resulted.

The NAS also considered the results of the two studies, as well as data from a study conducted in New Zealand in the 1980s. The study was similar to that conducted in the Seychelles—hair measurements, age 6, same neuropsychological tests. The results differed however, according to Dr. Jacobson. Whereas the Seychelles study found no adverse effects, the New Zealand study did.

Dr. Jacobson explained that NAS determined that the benchmark analysis chose the development endpoint as a guide from the Faroe Islands study. He noted that the EPA reference dose is based on this assessment.

Dr. Philippe Grandjean, Faroe Islands Study, described the Faroe Islands study for Committee members. A difference between the Seychelles study is that pilot whales are taken for food on a periodic basis in the Faroe Islands and eaten fresh and dried as pemmican. The whale meat provides an extra supply of fatty acids, proteins, and vitamins, as well as high exposure to methylmercury and PCBs. Dr. Grandjean described the exposure to whale meat as a natural experiment with spiked levels of methylmercury exposure up to 1,000 times higher than the lowest level of exposure.

Dr. Grandjean described the Faroe Islands as a homogeneous, wealthy, industrialized, Nordic fishing community; the participation rate was approximately 90 percent. Average fish consumption was three fish dinners a week, with whale meat eaten once or twice a month. Dr. Grandjean reported that exposure was only weakly associated with confounders.

The Faroe Islands study collected data on neurobehavioral effects on attention, memory, language, visual-spatial, and other functions, i. e., blood pressure and growth. Children were tested at age 7, with preliminary results at age 14 supporting the earlier findings. The Faroe Islands have one of the highest birth weights in the world, he noted, possibly due to the intake of high levels of DHA from fish, which may be extending the duration of pregnancy. He also reported no affect on postnatal weight gain from methylmercury.

The study used three factors to analyze methylmercury exposure: cord blood, hair, and a questionnaire that asked how frequently pilot whale meat was consumed. The coefficient variation was 30 percent—much more than the anticipated 5 percent. Cord blood was found to be the best predicator of adverse effects, with attention and language being the most sensitive neurobehavioral. He also noted that children with high exposure to methylmercury weighed about 1 k less at 18 months. In addition, Dr. Grandjean reported that the less precise the exposure, the more the effects are underestimated, and the impact is less when the exposure is stable or the interval between peak exposures is wide.

Dr. Grandjean noted that the study used highly skilled professionals to give the tests, but nevertheless it was difficult to do the complicated tests the same way each time. Some tests could not fit into time factors and were moved or administered differently. He also noted that tests must have as many possible outcomes as possible because the effects that are measured are subtle.

Dr. Gary Myers, Seychelles Study, stated that the hypothesis of the study was that prenatal exposure to methylmercury from maternal fish consumption during pregnancy might adversely affect children's developmental outcomes. The Seychelles was selected because the population consumes a large number of fish meals—up to 12 each week. The Seychelles have free universal healthcare and education, a low infant mortality rate, a 98-percent immunization rate, limited poverty, no malnutrition, and low levels of contaminants—PCBs below detectable limits, lead below 10 ug/dL, and low pesticide levels.

Methylmercury exposure was tested in maternal hair with the average exposure 7 ppm (range 1-27 ppm). More than 700 children were examined on five occasions from 6.5 to 107 months. Maternal covariates included maternal IQ, home environment, age, smoking and alcohol use, health history, and language spoken in the home. Child covariates included gender, hearing level, health history, birth weight, gestational age, birth order, and length of time breastfed. Tests were conducted by trained testers and, on a weekly basis, an evaluation by one evaluator was scored independently by a second evaluator while the test was given. The intra-class correlations were then computed to validate scores. About 10 percent of the tests were given by the investigators. Sessions were observed in situ or videotaped, and kappa statistics were computed.

Dr. Myers reported that results from infancy tests showed the expected results of the covariates with modest R^2s consistent with other development studies. No adverse associations were seen between prenatal exposure and any endpoints at 6, 19, and 29 months. Activity levels in boys at 29 months did decrease with increased methylmercury exposure (at subject endpoint). Results at 107 months again showed the expected effects of the covariates, modest R^2s, and only one adverse association out of the 21 endpoints (decreased activity levels) but the significance of this association was unclear. The study results found that exposure to methylmercury was below the toxic threshold.

According to Dr. Myers, the source of exposure is approximately same as in the United States, where the methylmercury concentrations in fish are similar to the fish consumed in the United States. Exposure measured in hair is estimated to be 10 to 20 times that in U.S. populations.

Dr. Christopher DeRosa, Agency for Toxic Substances and Disease Registry, noted that the ATSDR is affiliated with the Centers for Disease Control and Prevention and is the primary agency dealing with the implementation of superfund site cleanups. ATSDR has a mandate to prepare toxicological profiles on each priority pollutant, and to conduct initial research to fill data gaps for each substance. The ATSDR prepares public health assessments for each superfund site designated or recommended for inclusion on the NPL and updates profiles on pollutants at least every three years. The ATSDR also prepares public health assessments for

each site, including health outcome data, environmental monitoring data, toxicological profiles, and public concerns.

Dr. DeRosa reported that ATSDR released its first profile on mercury in 1989 and updated that profile in 1993 using the Iraqi data. The ATSDR convened an expert panel in 1994 to discuss benchmark data, but put the panel's work on hold pending the release of the Seychelles data. Relying on the findings of the workshop convened in Raleigh, NC, the ATSDR released an updated mercury profile covering all types of mercury to the public in 1999.

Dr. DeRosa explained several health guidance terms. He defined an MRL as "an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk." Acute is defined as less than 14 days, and intermediate as 15 days to a year.

Minimal risk level (MRL) is NOAEL (no observed adverse effect level)/LOAEL (lowest observed adverse effect level)/ BMD (benchmark dose)/UF (uncertain factor).

The ATSDR's MRL is 0.0003 ug/kg/day, using an uncertain factor of 3, which reflects two integrated components—1.5 for pharmacodynamics/pharmacokinetics and 1.5 for the possibility of domain-specific effects, such as those seen in the Faroe Islands study. The ATSDR's MRL derivation considerations include mercury ingested by mothers, offspring age group, hair-mercury levels in mothers, hair-to-blood concentration ratio, and blood-concentration-to-daily-intake measurements.

Dr. Penny Kris-Etherton, Department of Nutrition, Penn State University, urged the Committee to balance the benefits of fish consumption with the possible risks to pregnant women and women who may become pregnant. She reported that the American Dietetic Association and the USDA/DHHS both recommend individuals eat 2 to 3 fish meals per week and that the American Heart Association recommends eating 2 fish meals weekly to reduce the risk of coronary heart disease and receive the benefits of the omega-3 fatty acids contained in fish. She also noted that the benefits of fish consumption include reduced arrhythmias, anti-platelet effects, lowering of triglycerides, reduced coronary disease morbidity and mortality, and a decreased incidence of sudden death.

Because the FDA is seen as a safety net for the public and as a credible source of information, the FDA must provide multiple lines of dissemination for its methylmercury advisory that will meet the needs of individuals who want more technical information, as well as those that want a simple, uncomplicated message. She suggested a 1-888 number for consumers to get more specific information. She also urged the FDA to work with professional organizations and federal agencies to put out a consistent message using plain, clear language. The initial message should be short and simple, she said, with opportunities for additional information available. The message also needs to be positive—enjoy two servings of fish weekly, eat a variety of fish, and cook fish using healthy preparation techniques.

Dr. Susan Schober, Centers for Disease Control and Prevention, presented data collected from the National Health and Nutrition Examination Survey (NHANES), which assessed the health and nutritional status of adults and children in the United States during the 2-year survey period

1999-2000. Designed to monitor trends in health, risk behaviors, and environmental exposures over time, the NHANES data contains a mercury component in which children age 1 to 5 years and women age 16 to 49 years were tested for blood mercury levels.

NHANES also collected demographic data and data on fish and shellfish consumption in the U.S. The data on fish and shellfish consumption was recall-based, asking: "During the past 30 days did you eat any types of fish (shellfish [asked separately]) listed on this card? Include any foods that had fish (shellfish) in them such as sandwiches, soups, or salads." The cards included a list of specific species and "other" and "unknown" categories. Using a calculation of percentiles and geometric means that take into account weights, oversampling, and nonresponse, as well as standard errors for the complex sample design, the survey produced the following data. The data is based on 2-years' sampling. NHANES is an ongoing activity with data releases scheduled every 2 years.

Detection limit for total mercury: 0.14 ug/L			
Detection limit for inorganic mercury: 0.4 ug/L			
No levels found in women 16-49 years at or above 58 ug/L; 7.8% (95% C.I. 5.0%, 10.5%) at or above 5.8 ug/L			
Blood Mercury (ug/L)	**Geometric Mean[1]**	**90th Percentile[1]**	**95th Percentile[1]**
Children 1-5 years	0.34 (0.30-0.39)	1.31 (0.69-1.92)	2.28 (2.00-2.56)
Women 16-49 years	1.02 (0.85-1.20)	4.84 (4.11-5.57)	7.13 (5.79-8.48)

[1]95% confidence interval (C.I.) in parenthesis.

Ms. Caroline Smith DeWaal, Center for Science in the Public Interest, called for a stronger stance from the FDA on methylmercury standards governing commercial seafood and more rigorous communications to inform the public of the risks from exposure to methylmercury in fish and seafood. Ms. DeWaal cited the "fragmented and ill-equipped" structure of the federal food-safety regulatory system as unprepared to meet the challenge of protecting women at risk, and ineffective as it puts the burden of protection on the consumer. Ms. DeWaal noted that three federal agencies have adopted three different standards for exposure to methylmercury from fish and seafood.

She noted that the National Academy of Sciences, in its *Seafood Safety* report in 1991, criticized the FDA relying on the lowest blood level of mercury reported to produce effects in adults, rather than its typical approach, which is to base its analysis on the dietary intake level where no effects are observed. [Institute of Medicine, *Seafood Safety*, (Washington, DC: National Academy Press, 1991), pp. 196-197.] In addition, the FDA's advisory recommends consuming up to 12 ounces of fish per week, while the EPA advisory for freshwater fish recommends up to 6 ounces per week. These messages, according to Ms. DeWaal, are confusing to the consumer and place the burden on the consumer to determine what exposure levels are safe and to whom and when they apply.

Ms. DeWaal called on the FDA to adopt the EPA's standard for methylmercury as an action level and to initiate rulemaking to adopt a regulatory limit for methylmercury that fully protects the children of women who are or may become pregnant. In addition, on behalf of the Center for Science in the Public Interest, she urged the FDA to conduct monitoring for methylmercury in

commercial seafood and to include tuna as a fish that should be limited in pregnant women's and children's diets. Ms. DeWaal cited the NAS 2000 report that endorsed EPA's standard of 1 ug/k BW/day as scientifically justifiable, and noted that according to that report 60,000 U.S. children are born at risk of developmental problems due to methylmercury exposure *in utero*.

Dr. James Heimbach, ENVIRON, reviewed the nutritional benefits associated with fish consumption, including dietary guidelines issued by the American Heart Association and the American Dietetic Association. Dr. Heimbach explained the equation for estimating exposure to a food constituent or contaminant as: concentration x consumption. With this equation as its basis and data from two Continuing Survey of Food Intakes by Individuals reports by CSFII, Dr. Heimbach attempted to replicate the NAS' finding in its 2000 report that more than 60,000 newborns annually may be at risk for adverse neurodevelopmental effects from *in utero* exposure to methylmercury. Using a Monte Carlo analysis, Dr. Heimbach determined that the NAS figure for at-risk newborns was excessive and that at current levels of fish consumption, based on data from NHANES and the National Eating Trends Survey, which showed fish to be an infrequently eaten food, FDA's current advisory is adequately protective of pregnant women and their newborn children, including those who are heavy consumers of fish. Dr. Heimbach reported that the exposure data do not suggest a need to revise the current FDA advisory, and do not suggest a need to advise women to avoid or limit consumption of species of fish other than those already listed.

Mr. Harvey Clewell, ENVIRON, presented findings on the evaluation of the Environmental Working Group's 2002 analysis of maternal blood levels that could be achieved during pregnancy. Using a pharmacokinetic model that includes both maternal and fetal compartments and describes the changes in maternal and fetal tissues and maternal dietary intake that occurs over the course of pregnancy and gestation, Mr. Clewell attempted to replicate the findings of the EWG. He said he could not replicate the results for the first scenario based on the consumption of 12 ounces of fish per week using the documentation provided in the EWG's pamphlet, "Brain Food." The results for the second scenario, which describes eating a single type of fish, were replicated closely, though the model produced much lower blood-level estimates. In summary, Mr. Clewell noted that maternal blood concentrations might sometimes exceed RfD blood concentration levels for worst-case exposure scenarios, but that the use of the RfD as a "bright line" for evaluation of safety is not appropriate. Instead, he noted that realistic exposure scenarios result in maximum blood levels within a factor of three of RfD and are well below those of the Faroe Islands data that were used to determine the RfD. He disputed the NAS report's finding that 60,000 children are born at risk in the United States each year, saying that the data used to reach this figure were based on an average of three 24-hour dietary recalls, which is not an estimate of usual intake. The figures, he said, represent an over estimate for those women and for the average consumption of all women.

Guest Speaker Presentations (Wednesday, July 24)

Dr. Elizabeth Southerland, Environmental Protection Agency reported that mercury is the number one pollutant in lakes monitored by the EPA and has been for the past 9 years. Reviewing the different standards used by federal agencies for mercury toxicity, Dr. Southerland

noted that several states have taken responsibility for developing their own advisories, with 11 states issuing combined advisories for both recreational and commercial fish. Nine of these states have included tuna in their advisories, a fish not mentioned in FDA's advisory. Coastline advisories issued by states on the Gulf Coast and East Coast also refer to marine fish caught as recreational fish. Dr. Southerland noted that 28 states use the ATSDR's RfD of 0.3 ug/kg BW/day as the minimum RfD for adults and 27 states use the EPA's RfD of 0.1 ug/kg BW/day for children as the minimum standard. The formula values for calculating the EPA mercury advisory, according to Dr. Southerland, are:

- Hg reference dose (RfD) = 0.1 ug/kg BW/day
- Consumer body weight (BW) = 65 kg (estimated woman's body weight)
- Meal size = 8 oz. (uncooked weight)
- Concentrations (C) Hg in fish (states) = National List of Fish and Wildlife Advisories

$$\textit{Maximum daily fish consumption rate (kg/day)} = \frac{RfD \times BW}{C}$$

Dr. Southerland also showed a table used to determine recommended fish meals per month based on methylmercury fish tissue levels. She also provided a chart showing the mean mercury concentration in tissues of selected fish species, noting that the data came from 8,000 stations in 44 states and that a minimum of 100 tests were conducted for each species of fish. Almost two-thirds of the 23 freshwater species listed would provide more than 0.16 ppm per meal. [Source: NLFWA February 2002, data from 1987-2001.]

Dr. John Middaugh, Alaska State Department of Epidemiology, spoke to the Committee about the dangers of the FDA's "one-size-fits-all" approach to methylmercury advisories, noting that FDA's recommendations for fish consumption are not consistent with Alaska state recommendations. Dr. Middaugh reported that public health advisories are having an adverse effect on Alaska Natives and rural resident subsistence consumers who have few alternatives to fish. The result is that Alaska Natives and rural residents are consuming less fish, despite state advisories that they should maintain their traditional diet. As a result, the state is seeing an increase in diabetes, heart disease, and other illnesses. Dr. Middaugh noted that Alaska state data provide evidence that most, if not all, Alaskan exposures to methylmercury are below those of current concern, even applying conservative models, based on extensive sampling of fish species from Alaska waters. Salmon, he noted, has shown the lowest levels of methylmercury, ranging from non-detectable to 0.05 ppm.

Dr. Middaugh described several major dietary surveys underway in Alaska and new data from the Alaska Native Maternal-Infant Cord Blood Contaminants Study, conducted by Dr. James Berner, that measures actual human exposure levels. The state initiated a statewide maternal hair mercury biomonitoring program in June in which pregnant mothers from throughout the state can send in a hair sample for testing. This will provide data from throughout the state and allow the state to take immediate action should samples from a particular area show increased methylmercury levels.

Alaska, in consultation with the FDA, developed the following language, which it continues to support, "Some kinds of fish that are known to have much lower than average levels of

methylmercury can be safely eaten more frequently and in larger amounts. Contact your federal, state, or local health or food safety authority for specific consumption recommendations about fish caught or sold in your area." In addition, the Alaska Division of Public Health issued consensus recommendations for fish consumption in Alaska: "The Alaska Division of Public Health continues to strongly recommend that all Alaskans, including pregnant women, women who are breastfeeding, women of childbearing age, and young children continue unrestricted consumption of fish from Alaskan waters." Dr. Middaugh reported that Alaska does not support national advisory recommendations that restrict fish consumption to 12 ounces a week or recommend that pregnant women restrict fish consumption to one meal per month.

Dr. Charles Lockwood, Department of Obstetrics & Gynecology, Yale University School of Medicine, spoke to the Committee as the former chair of the American College of Obstetrics and Gynecology (ACOG). He stated that he and his colleagues are confused by the different advisory messages and are having a difficult time getting the appropriate message to their patients. They have been urging patients to eat fish for the past 10 years, but are now concerned that they don't know enough about the effects of methylmercury on fetuses to effectively warn their patients. He asked the FDA to conduct research to assess the effects of methylmercury on fetuses, including epidemiological studies to get a sense of the correlation between fetal exposure and subsequent neurological effects. He also urged the Committee to err on the side of being conservative.

Dr. Lockwood asked for a single federal guideline that included regional and species-specific warnings so that physicians don't have to interpret different state and federal warnings. Dr. Lockwood offered to work with the FDA to incorporate the advisory in direct mailings and in published handouts distributed to physicians' offices. When asked by Committee members, he indicated that he thought his colleagues would participate in a national monitoring program of pregnant women.

Dr. Diana Zuckerman, National Center for Policy Research for Women and Families stated the FDA's current efforts to protect the American public from the health risks of methylmercury are not adequate to protect the public or to educate them so that they can protect themselves. She listed three concerns:

- The FDA does not adequately monitor methylmercury levels in commercial fish supplies.
- The FDA advisory is incomplete and should be revised to include information about tuna based on the amount of tuna consumed by the public.
- Information about methylmercury exposure has not been disseminated adequately to consumers.

Dr. Zuckerman expressed surprise that the current FDA advisory does not include tuna. Consumer groups strongly urge that canned tuna be included in the advisory based on the quantity of tuna consumed by the American public. The U.S. Tuna Foundation estimates that, on average, the 1 percent of women who eat the most tuna eat almost 7 ounces a week, just slightly below the 9 ounces that FDA scientists consider the upper limit of what is safe for pregnant women. Dr. Zuckerman offered several suggestions for getting the message out to consumers:

- Include benefits and risks
- Make the warning to nursing mothers and young children more visible in the message
- Include the advisory in women's magazines, parenting magazines, TV PSAs, and on menus and all fish products sold, including canned tuna
- Provide labels on fresh fish packages as well as frozen and canned fish products

In conclusion, Dr. Zuckerman called on the FDA to set a regulatory limit for methylmercury of 0.1 ug/kg/day, which is the EPA standard, and to monitor levels of methylmercury in shark, swordfish, king mackerel, tilefish, and fresh and canned tuna, and remove them from the market if those levels are violated.

Mr. Richard Wiles, Environmental Working Group, said that the EWG is "deeply troubled by the FDA's antiquated exposure and risk assessment models for methylmercury and the undeniable fact that they have produced a mercury health advisory for pregnant women that allows thousands of unborn children to be exposed to unsafe mercury levels each year." Mr. Wiles called on the FDA to conduct its own risk assessment through a public and transparent process, and to issue a comprehensive list of fish that women should avoid during pregnancy as well as a list of fish that are low in mercury and high in omega-3 fatty acids that women should eat more of during pregnancy.

Mr. Wiles asked the FDA to change the way it looks at fetal risks from methylmercury exposure. He suggested the agency work to protect 99 percent of pregnancies, instead of the current FDA model based on the 90^{th} percentile. In addition, he called on the FDA to:

- Adopt the NRC blood level for methylmercury.
- Conduct a one-time sample of the top 40 or 50 most consumed fish so that the agency is operating from a position of knowledge when advising pregnant women on fish consumption.
- Conduct and make public a state-of-the-art exposure and risk assessment of fetal mercury exposure.
- Issue a mercury health advisory that protects 99.9 percent of pregnant women from methylmercury, while at the same time recommending fish and other foods that are low in mercury and high in omega-3 fatty acids.

Ms. Jane Houlihan, Environmental Working Group, addressed the question: What would happen if a pregnant woman followed FDA's advice and ate 12 ounces of fish a week, excluding shark, swordfish, king mackerel, and tilefish? According to the model presented by Ms. Houlihan, if women were to follow FDA's advisory and eat 12 ounces of "safe" fish a week, more than a quarter of all pregnancies would be exposed to mercury at levels above the reference dose for at least a month of pregnancy.

The Monte Carlo model relied on by Ms. Houlihan used a probabilistic method that allows for a full accounting of biological variability, differing individual consumption patterns, and a range of mercury concentrations in seafood. The model relied on data from NHANES and measurements of human variability in mercury absorption and excretion capabilities as well as a nonsteady-state (transient), one-compartment pharmacokinetic model developed and verified by

Dr. Gary Ginsberg of the Connecticut Department of Public Health. Consumer patterns were modeled using the CDC's newly released 30-day recall seafood consumption study and the National Eating Trends database from a major market survey research organization. Mercury concentrations in seafood were based on compilation data from seven government databases of mercury in fish tissue from FDA, NOAA, EPA—a total of 50,000 samples.

Based on the results of the model, Ms. Houlihan reiterated the recommendations to the FDA made by her colleague Mr. Wiles.

Dr. Henry Anderson, Wisconsin Division of Public Health, described the work Wisconsin has done to inform its citizens of the risk of methylmercury exposure from eating fish caught in state waters. The state issued its first methylmercury advisory in 1975 using the FDA market fish advisory as a reference.

The current advisory, issued in 2000, targets primarily anglers and their families with a goal to provide anglers with a qualitative comparison to market fish based on risk assessment, rather than a quantitative comparison. The advisory gives consumers species they can eat, not which species should be avoided. The state also set its own levels for consumption based on the contamination levels in the fish.

The Wisconsin advisory is specific in its recommendations. Using pictures and an equation format, the advisory, entitled "A Woman and Child's Guide to Eating Fish from Wisconsin," says:

- Weekly—One meal per week of canned light tuna (6 ounce can = 1 meal) and 1 meal per week of either bluegill, sunfish, black crappie, white crappie, yellow perch, bullheads or any commercial fish (fish you buy in a store or restaurant)
- Monthly—One meal per month of any sport fish species (sport fish are any fish you catch or are given, such as bass, walleye, northern, perch, or crappie). Sport fish are NOT fish you purchase in a store or restaurant.
- Never—Eat any swordfish, shark, king mackerel, or tilefish.

Dr. Anderson called for increased commercial fish monitoring, increased human biomonitoring, and continued research on health effects, especially potential cardiovascular effects. He noted that advisories must inform consumers of the risks as well as the benefits of fish consumption.

The state's one-line message is, "Hook Into Healthy Fish." The pamphlet includes pictures of fish common in Wisconsin waters with a scale below each picture showing general mercury levels. A recipe and additional information is offered to those who call the local health department.

(Dr. Anderson asked the Committee to recognize that the design of the Wisconsin state advisory is from the Maine state advisory.)

Mr. Michael Bender, The Mercury Policy Project, recommended that the FDA develop effective surveillance, monitoring, testing, enforcement, and consumer programs for methylmercury in commercial seafood in conjunction with consumer groups, the fishing industry, and appropriate federal, state, and local government agencies. Mr. Bender noted the need for data to be collected

using state-of-the-art testing methodologies, approaches, and equipment, and for fish size to be included as part of a comprehensive seafood testing protocol.

Mr. Bender also called on the FDA to establish a regulatory limit for methylmercury in seafood that is fully protective of the U.S. population and, in particular, women of childbearing age, pregnant and nursing mothers, and children. He also asked that the FDA expand its list of "do not consume" seafood known to have high mercury levels to include canned tuna and marlin. Mr. Bender noted that 10 states now include tuna/canned tuna in their advisories—some dating back to 1997—with recommendations about the quantity of tuna that should be consumed per week by pregnant women, and in some cases children.

Noting that a March 27, 2002 briefing statement from the National Marine Fisheries Service recognizes that "subsistence, commercial, and marine recreational fishermen and their families represent a new subpopulation of the seafood consuming public that will likely require additional safeguards in order to protect them against excessive methylmercury ingestion via seafood," Mr. Bender called on the FDA to issue an advisory to this subpopulation that particularly addresses their risks.

Mr. Bob Collette, National Fisheries Institute, and Dr. William Connor (on speakerphone), Oregon Health and Science University, presented a collaborative review of the positive role fish and seafood has on the nutrition and health status of U.S. consumers. The National Fisheries Institute (NFI) believes the FDA advisory is an effective tool for disseminating this information and is assisting the FDA by including it on their website. Mr. Collette noted that fish is a good source of protein, B and B12 vitamins and selenium, and is low in saturated fat and calories. He noted that fish and shellfish are better sources of DHA than other animal sources. He also noted that Omega-3 fatty acids are necessary from conception throughout one's lifespan, that they are components of membrane phospholipids, and that in their absence, the body replaces them with other fatty acids that are not as beneficial.

In summary, Mr. Collette said that health benefits from fish could be lost if a higher reference dose is recommended. He asked that consideration be given to the negative impact of warning labels and to pursuing zero risk in the advisory, noting that at some point will fish be seen as too scary to eat. He also cautioned the Committee about putting warning labels on canned tuna, noting that there are few substitutes that provide the same benefits. Finally he cautioned the Committee about including alternate fish, noting that some alternatives are under restricted fisheries management control.

Public Speaker Presentations (Tuesday, July 23)

Dr. Rhona Applebaum, National Food Processors Association (NFPA), stated that NFPA believes the FDA looked at the totality of the evidence and the data available, and then made a risk management decision and produced a risk communication message that provided the facts to consumers, as well as the necessary advice on methylmercury and fish consumption. In conclusion, Dr. Applebaum stated that NFPA believes FDA has done an exemplary job in the development, focus, and wording of the advisory.

Dr. Richard Fisher, dentist and private citizen, applauded the Committee for its work to communicate the risk of methylmercury exposure through fish consumption to consumers. He asked Committee members to contact their colleagues and lobby for the elimination of mercury amalgams as cavity fillings, citing the propensity of the mercury to be absorbed by the brain and converted into inorganic mercury. He noted that mercury amalgam fillings contribute four times more mercury in the body than diet. He also noted that substantial amounts of mercury enter municipal wastewaters from dental offices, which in turn pollutes the aquatic marine environment.

Jae Hong Lee, M.D., M.P.H., National Center for Policy Research for Women and Families, said that the FDA's current efforts to protect the public are inadequate based on flawed rationale and its failure to effectively disseminate information about the health risks of methylmercury to the public. Dr. Lee reported asking if the FDA was monitoring levels of methylmercury in fish. He said FDA contends that levels of methylmercury in fish do not change over time and that historical data were relevant today. Dr. Lee expressed his disagreement, saying historical data does not hold over time because environmental factors change and that commercial products should be monitored on an ongoing basis.

Dr. Lee said that canned tuna makes up 75 percent of the fish consumed in the United States and, because of the sheer quantity consumed, is the most likely source for exposure to methylmercury. He suggested that canned tuna be labeled and included in the advisory. He also noted that the advisory should be placed where consumers will see it—on the fish package. If the FDA believes canned tuna should be limited to 9 ounces per week, he said, put that on the label.

Committee-Member Led Discussions

Dr. Miller asked three Committee members to address specific discussion areas prior to the Committee addressing the FDA's questions.

Toxicology Discussion led by Dr. Fischer. Dr. Fischer addressed the question: what is toxicology of methylmercury? The toxicity of methylmercury is under study at this time, Dr. Fischer reported, with the molecular mechanisms that cause alterations to the nervous system not being well understood. Animal studies indicate that granual cells in the brain may be the primary target of the toxin. Dr. Fischer noted that there are studies underway in the United States that are investigating the synergy between methylmercury and PCBs. A paper on the synergy between methylmercury and PCBs reports that the release of dopamine, a neuro transmitter, from isolated brain tissue is greater when both methylmercury and PCBs are present than from methylmercury or PCBs alone. In situations where there is no effect from methylmercury, there is a greater response in the release of dopamine when PCBs are added. The paper also found that there is a greater amount of free calcium released when both methylmercury and PCBs are present. These findings could indicate that methylmercury is increasing the toxicity of PCBs—effecting the release of dopamine and free calcium in cells but, it is unclear which chemical is augmenting the toxicity of the other. He noted that the relevance to the Committee's work is low because the tests are using elevated levels of methylmercury and PCBs.

Dr. Fischer reported that there is not sufficient data to determine when the risk is greatest to the fetus. He said that it may be later in the pregnancy, though that is suspicion only. He also said that there may not be a threshold for the effects of methylmercury, and that there probably is some effect at low levels of methylmercury. If this is the case, he noted, these might be attenuators of the human's ability to live with these effects, which is how they may have to be thought of in the future.

Dr. Fischer expressed his belief that more monitoring of human exposure is needed, even if it means taking money away from measuring methylmercury in fish. He noted that accurate measurements are available from hair samples—more accurate measurements than guessing about fish consumption. The bottom line, said Dr. Fischer, is that we don't know the target concentration. The concentration-response relationship is needed.

Discussion among Committee Members on Toxicology. Given the uncertainties, the FDA must reduce exposure to the lowest possible level without banning fish consumption. The FDA's position must be that there is not a threshold. More data is required so that decisions can be made based on the best data available.

More data is needed on how cord blood methylmercury levels relate to maternal blood methylmercury levels. If the cord blood methylmercury level is 50 percent higher than the maternal blood level, then the data needs to be adjusted to consider this.

More research is needed on mercury toxicology—considering all types of mercury exposure and the transformation of mercury in the brain from organic to inorganic. Research to determine the dose we should be concerned about is needed. Consideration should be given to children and that FDA's approach should be conservative.

More research is needed on the issue of maternal blood volume and what affect this has on methylmercury levels. More knowledge about the beneficial affects of DHA also would be helpful.

Additional research needs to be done to investigate the relationship between methylmercury and PAHs found in the sediment of lake and river bottoms. PAHs are dioxin like. Dr. Fischer responded that PCBs are non-dioxin and that there haven't been any findings for dioxins compounds.

It was noted that children are not small adults and the FDA should consider rewording its advisory to address children. Committee members agreed there should be concern about young children, but some felt the FDA wording covered children in its advice to pregnant women. Because neuro development continues after birth, the advisory should extend to lactating women. The portion size of 12 ounces, if it applies to children, should be related to body weight.

Consumption Discussion Led by Dr. Dwyer. Dr. Dwyer noted that the consumption amount of a specific food x the frequency that food is eaten x the concentration of the substances must be calculated before one can consider if all relevant factors and information have been addressed in

the fish advisory. The amount of fish consumed, she noted, depends on portion size and the number of servings eaten over a time period.

The common names of the fish on the advisory need to be used so that consumers can recognize the fish. The FDA needs data on fish that are major contributors to the total dose of methylmercury. The advisory, she suggested, needs to mention fish that are major contributors to the total dose of methylmercury a person has, not just the fish with the highest levels of concentration. The advisory also needs to emphasize variety and substitution, not just avoiding fish for high-risk groups. She noted that to avoid the "good fish-bad fish" approach, the advisory should stress the benefits of eating fish and of eating a variety of fish.

Dr. Dwyer suggested that the FDA prepare a hazard analysis and then set the level in the advisory accordingly—possibly lower or higher than the current 12 ounces a week for pregnant women if the data support it. The FDA needs to give transparent evidence—the assumptions and the math—as evidence for the decision. She also noted the need to monitor hair and cord blood levels, perhaps for merconium as well as methylmercury.

In conclusion, Dr. Dwyer noted that the FDA needs to collaborate with other federal agencies and state and local health departments to get the consumption message across.

Discussion among Committee Members on Consumption. When preparing an advisory that includes children, it is more helpful to define by age than weight. Most state advisories make recommendations for children under the ages of 12 or 14. It was also noted that it would be helpful to add some dimensions to the consumption data, such as geographic area, demographics, and ethnic descriptions, to reach those subpopulations that are major consumers of fish.

Risk Communication Discussion Led by Dr. Scherer. Dr. Scherer simplified the framework for delivering a risk-communication message to six steps. The goal of the advisory is to create sustainable change. He noted that protective change is very difficult to accomplish, and that evaluation at each stage is appropriate to determine the effectiveness of the process.

Step 1. Deliver the message using news media, physicians, etc. Dr. Scherer noted that these sources of dissemination are reaching a lot of people who already are within the guidelines, but because not much is known about the target audience—those in the 95th percentile—they are harder to reach. As an example, Dr. Scherer suggested this step reaches 100 people with the message.

Step 2. Attract the consumers' attention. Something in the message has to make the consumer pay attention. Continuing the example, Dr. Scherer estimated that at this step the message has caught the attention of 50 of the 100 people reached in step 1.

Step 3. Help the consumer understand the message. This is a complex message that requires the consumer to make judgments. An estimated 25 of the 50 consumers reached in step 2 understand the message.

Step 4. Recall the message. Consumers have to recall the message each time they are in a store or restaurant. An estimated 12 of the 25 consumers reached in step 3 recall the message.

Step 5. Retain the behavior. Consumers decide to make a change based on the information. At this point, the message needs to be repeated over and over again so the consumer doesn't have to think about it. An estimated 6 of the 12 consumers reached in step 4 retain the behavior and chose not to eat the four fish in the advisory.

Step 6. Demonstrate the behavior. Most people operate on simple rules that are based on simple decisions, noted Dr. Scherer. The advisory needs to be an aid to this rule so it becomes part of the general rules people follow. An estimated 3 of the 6 consumers reached in step 5 demonstrate the behavior and follow the advice.

In this simplified version of the process, in the end only 3 of the 100 people who originally received the message demonstrated a behavior change and decided to follow the advice in the advisory.

Discussion among Committee Members on Risk Communication. People want different levels of information. Some segments of the fish-consuming and pregnant-women populations might want advanced levels of information.

Behavior change occurs over a long period of time so change is difficult to measure. The best results occur when the message is focused on a target population. When people are faced with a mixed message, such as contradictory messages from the EPA, FDA, and states, they often disregard all messages. There are more than 2,000 fish advisories currently in the United States. Labeling is successful for a certain portion of the population, but is only part of the process. Labels have more of an effect on simple behaviors.

Sustained behavior changes require that the message be received multiple times, which requires the use of all types of media and different delivery sources.

Science must be put into the complex message. There needs to be enough information to help people make judgments about risks and benefits. If the message is too short the benefit part of the equation is missed.

Regarding tuna, the message must be carefully crafted or consumers may stop eating tuna. This is a difficult consideration because tuna is an important part of the diet for many consumers

Committee Conclusions/Recommendations

1. Has the agency adequately addressed and appropriately considered all the relevant factors and information that bear upon the elaboration of a consumer advisory on fish consumption? Are any factors not relevant? Are there additional factors that would be relevant?

Committee Recommendation: The advisory should continue while additional data are gathered. It was recommended that FDA conduct and publish its risk assessment in peer review literature along with the results of competing models and let the scientific community be the final arbiter. It was recommended that the advisory include children more than it now does and have more prominent information for young children (age 1-12 or 14). It was recommended that the FDA and EPA produce a combined message and collaborate to get the message out to the public. The Committee agreed that all possible avenues should be used to disseminate the message, including retailers.

Committee Discussion: Several questions were surfaced including the appropriate model to use. Dr. Miller asked that the Committee focus on what relevant factors and information were left out of the advisory.

There was general feeling that the data on mercury levels in fish that are available were not presented and that some relevant data were missing. FDA recommendations made on the basis of average levels of fish that are not currently being monitored are a concern. There was a feeling that the FDA is advising the public prematurely, i.e., without adequate data. Numbers available now should be used as a baseline with more study needed. FDA should go to industry and other sources and get the numbers. It was agreed that the advisory should continue, and that more data are needed in order to have the information necessary to update the advisory in the future.

There needs to be a risk assessment on the effects of methylmercury in children. This has not been done. The focus has been on prenatal exposure.

2. Should the advisory have specifically advised pregnant women to AVOID any other species not specifically mentioned, and if so, what would be the scientific rationale?

Committee Recommendation: FDA should conduct an assessment on a priority basis regarding the impact of tuna on the methylmercury burden for pregnant women and children. At the same time, the FDA should issue a cautionary advisory for tuna, essentially saying that tuna should comprise "X" percent of a pregnant woman's diet, and that women should consider eating other varieties of fish during their pregnancy, with an appropriate cautionary message for children as well. The statement should be modeled on the Wisconsin literature. If the science changes the need for the cautionary statement, then the statement should be reconsidered. This recommendation also pertains to advice about what fish should not be eaten—update the advice as warranted by the science.

It was recommended that Dr. Scherer or someone with his qualifications be added to the project to work with the FDA's own risk communicators.

Committee Discussion: Dr. Miller asked, What other fish should be included?

The advisory should say fish consumption from at least two of these groups—two different species of fish in a week—not more than half the weekly allotment should come from a single variety.

Tuna was seen as the underlying issue in this question. The Committee acknowledged that data clearly indicate that tuna is the most highly consumed fish in the United States, but that the data do not show the contribution of methylmercury exposure in humans from tuna. Tuna was estimated to have a 23% market share. If that is correct, the Committee felt it is a significant enough that a specific recommendation may be warranted to limit tuna in the diet. No Committee member felt canned tuna should be banned. The question was what should replace it, given the possible implications of the replacement product.

The advisory should include tuna and a warning should be given for children to limit the consumption of tuna. NHANES data showing methylmercury levels in children age 1 to 5 are low is not relevant because children that age don't generally eat tuna. In the absence of knowing what is safe, potential risk should be addressed and included in the advisory.

The answer should be data-driven; not a good fish-bad fish position. Risk models need to be done. Data presented was aggregate or mean of methylmercury content, with light tuna is at the lower end of the range. Data that says how much tuna can be eaten and what type is needed. Data on tuna is available. Need to select the different populations that are eating tuna—i.e., pregnant women and school-age children—and do a risk assessment.

There is substantial evidence that excessive levels, levels that would be consistent with poisoning events, of methylmercury, harm children. There also is evidence that tuna is a major source of methylmercury. A cautionary guideline that follows Wisconsin's guideline would be appropriate. There needs to be more specific information in the advisory. Give details so people know why to follow the advisory. Risk communication must strike a balance when the message is complex.

3. Should the agency issue a fish listing as an adjunct to the advisory to clarify what is meant by a "variety" of fish?

Committee Recommendation: The Committee recommended that the FDA issue a fish listing that shows the methylmercury concentrations in the different species of fish. The Committee also agreed that the FDA should collaborate with the EPA to produce a list that includes all varieties of fish, both commercial and sport. All common names of the fish species should be used in the listing.

Committee Discussion: Dr. Miller asked if anyone objected to a fish listing. No one did. The list should contain different species of fish, not varieties of a single species. The list should emphasize the species with the lowest methylmercury levels, including shellfish. Collaboration with EPA could result in all fish being included in the list, not just marine or commercial fish now under FDA responsibility. The top 20 species should be readily available in the listing.

Consumers need a uniform advisory that has certain things in common and can be modified to meet particular local conditions.

4. Should the agency revise its consumer advisory to make explicit that the "12 ounces per week" includes all sources of fish, both recreational and commercial?

Committee Discussion: There was concern about the wording "12 ounces per week."

5. Should the agency increase its monitoring of methylmercury in commercial fish in order to keep this advice current?

Committee Recommendation: The Committee agreed that the FDA should increase its monitoring/collection of information on methylmercury exposure.

Committee Discussion: There is concern about asking FDA to spend resources to find out data they already know. FDA knows that methylmercury is in fish and the market basket survey gives information about what consumers eat. There is a preference for sampling of biomarkers and research to further test different messages on different groups. Not sure we have enough data on this issue; monitoring has not been adequate.

Monitoring of methylmercury exposure should be expanded to include children, pregnant women, and biomarkers. Need geographical data; a lot of demographic data is not available from NHANES.

Respectfully Submitted:

Catherine M. DeRoever

Catherine M. DeRoever
Executive Secretary
Food Advisory Committee

Certified:

Sanford A. Miller

Sanford A. Miller, Ph. D.
Chairman
Food Advisory Committee