

FDA may have forced itself to this position because of the decision on Red 2 which was based largely on the agency's finding that the data before FDA were not sufficient to support the safety of the color additive. Some of the colors were provisionally listed on the basis of the same kind of data used to support Red 2.

In the memo of the call to Lanese, Roberts reported that the Bureau is putting together detailed background information on colors for which toxicology questions exist, including Red 4, adding that this information will be reviewed with the Commissioner and General Counsel before a final agency decision is made about Red 4.

After expressing disappointment, Lanese asked whether the dog study should be abandoned, but Quinn advised that it would be in Lanese's best interest not to take this action. Quinn also asked Lanese to inform the PMA and the National Cherry Growers and Industries Foundation of the status of Red 4.

At the earlier meeting, industry officials had indicated that the only limiting factor in meeting the Sept. 30 date would be the ability of the contracting laboratory to initiate the study promptly and availability of the required test animals.

The industry officials discussed the testing procedures with representatives of FDA's Division of Toxicology and Division of Color Technology. FDA asked that the color used for testing purposes be certified by the agency, and sufficient material be reserved for future use.

PCB

PCB, PBB REPORT CALLS FOR MORE RESEARCH

A Department of Health, Education and Welfare subcommittee last week issued a report assessing the health effects of polychlorinated biphenyls and polybrominated biphenyls, calling for more research (See FOOD CHEMICAL NEWS, May 31, Page 38).

The inter-agency HEW group made no specific recommendations which would guide the Food and Drug Administration in reassessing the temporary tolerances for PCBs. The agency has been considering lowering the tolerance in fish from 5 p.p.m. to 2 p.p.m. (See FOOD CHEMICAL NEWS, June 21, Page 27; and July 12, Page 2). The Environmental Defense Fund has petitioned FDA to lower the PCB tolerances (See FOOD CHEMICAL NEWS, May 17, Page 50).

Discussing human exposure, the group said reports indicate "that a substantial proportion of the population of the U. S. has been exposed to PCBs," but that "minimal" exposure has occurred from food, air and water. The "significant human exposure," the report said, "appears to be limited to sports fishermen consuming fresh water fish from contaminated streams and lakes, and to occupational exposure in industrial workers."

MONS 083348

Kolbye Opposes "Zero" Tolerance for Contaminants

The chairman of the HEW panel, Dr. Albert C. Kolbye, Jr., Associate Director for Sciences of FDA's Bureau of Foods, recently opposed the concept of setting "zero"

tolerances for environmental contaminants which are carcinogenic. He stated his views in a paper co-authored by another member of the subcommittee, Dr. Frank Cordle, of the Bureau of Foods.

The paper, presented to the American Veterinary Medical Association in Cincinnati, O., noted public concern about "environmental carcinogens," saying, "... When one is dealing with contaminants already in food, such as PBBs, then the question is not banning the addition to food of a particular substance, but of banning food itself."

Explaining the rationale for §406 of the law, which covers unavoidable poisonous and deleterious substances, Kolbye and Cordle noted that "most natural foods or substances occurring naturally in the food supply have never been tested to see whether or not they could induce a carcinogenic response in test animals when fed at substantial levels in the diet."

Using aflatoxins as an example, the FDA-ers said that "if regulatory levels were set on a no detectable residue basis, the pragmatic effect would be to ban a major portion of the world's supply of corn, rice, and peanuts." They added:

"If a zero tolerance were to be applied to PCBs, almost all commercial freshwater fishing and a major portion of saltwater fishing would be wiped out. One might rationally ask what about residues of DDT, dieldrin, and other pesticide residues that contaminate food from environmental sources? Should these foods also be banned because of very low level residues? The obvious answer is that it would be impossible and lead to chaos in the American food market."

Kolbye and Cordle said, "Zero tolerances are pragmatically impossible to set for most environmental contaminants as far as food is concerned."

Noting that a committee appointed by the Governor of Michigan in effect recommended a zero tolerance for PBBs, the FDA-ers said "there is ample evidence that most of the low-level contamination presently occurring in farm animals and other farm products in Michigan is from indirect causes including environmental and other unavoidable sources in spite of good agronomic practices." They added that "we cannot eliminate all PBBs by simply declaring them as a banned substance."

The "question" in Michigan, Cordle and Kolbye said, "is one of how much food to ban which also translates directly to the question of how many livestock to destroy and bury." They continued:

"As a regulatory guideline is lowered, additional livestock herds will become illegal, thus requiring destruction of entire herds based upon samples taken from some but not all animals in that herd. In order to maintain a 95% confidence that no violative residues will occur,

the sampling characteristics involved will undoubtedly lead to a point where largely unaffected herds may have to be destroyed because of detection of low level trace residues in some animals. The only way this can be avoided will be sampling from each and every animal involved which would impose a tremendous burden on the already strained chemistry laboratories of the State of Michigan."

The FDA-ers noted that there is also a problem "of recontamination of new and previously uncontaminated herds due to low level accumulation of PBB residues picked up from the environment." For example, they said, "even if a new dairy herd were purchased from out of State and placed on a previously contaminated Michigan dairy farm, it is likely that these animals might develop detectable, albeit very low, residues of PBBs."

Describing how the action levels were set for PCBs and PBBs, Kolbye and Cordle expressed the belief "that the PCB and PBB problems are under appropriate control," urging that "we all should join in a combined effort to prevent human exposure to potential health hazards such as PCBs and PBBs."

The authors noted that PCB problems have occurred primarily in poultry, dairy cattle, and freshwater fish, explaining that poultry contamination occurred from feed contaminated with carbonless paper, heat exchange fluid or fish containing high levels.

"Due to various actions by FDA, we have not experienced further problems in poultry in the last few years," Cordle and Kolbye said. They added that "dairy cattle do present a problem because of contaminated silage from flaking silo sealants in areas where PCB sealants were used," and that "freshwater fish in various areas are a continuing major problem ..." The FDA-ers added:

"Today the PCB in food problem still exists, although on a much smaller scale with the exception of fish. PCBs in milk still occur from various contaminated dairy farms, and appropriate action is taken by FDA to protect the public. Fortunately, dairy milk usually represents inputs from many dairy farms, most of which are PCB free, and thus milk as it reaches the consumer usually has no detectable residues. Occasional sporadic exposures of humans to very low levels are likely to be of negligible consequence, but continuing efforts are necessary to reduce human exposure as much as possible. Fish, primarily freshwater fish, remain a continuing problem, especially as far as sportsfishermen who consume much of their catch are concerned. Several States have taken action to warn about consumption of such fish and FDA prevents fish containing residues above our action level from being sold in interstate commerce."

The PBB problem in Michigan resulted in a mixup in which a flame retardant product was mixed with animal feed. Kolbye and Cordle said that recent tests by Michigan and the Agriculture Department have shown of 769 beef cattle tested, 732 contained no detectable PBBs. Also tested were 885 dairy cattle, of which 808 contained no detectable residues, 66 contained residues below the guideline level, and 11 contained residues above the guideline. The FDA-ers said milk samples and dairy products sampled between December, 1975, and April 12, 1976, showed "no detectable residues."

"It is important to understand therefore that at current FDA guideline levels, the average Michigan resident could at most receive only very sporadic and occasional food exposures to very minute levels of PBBs," Kolbye and Cordle said.

PCB Exposure "Static" Until There is a Change in Fish Residues

The HEW subcommittee said that it appears that "PCB levels in the diet may have 'bottomed out' and may remain static until such time as there is a change in the PCB residues in fish." In FDA's Total Diet Studies, the only PCB residues have been found in the meat-fish-poultry composites. "The fact that levels in these composites have declined to only traces ... support the inference that the meat, poultry and eggs no longer contain detectable PCBs and that the low level findings are probably due to the fish in these composites," the report said.

National Marine Fisheries Service data is somewhat inadequate, the group indicated, but they do suggest "that the exposure of the population as a whole from PCB residues in ingested fish is probably well below 19 mcg/day/consumer, based on PCB levels which are estimated to be below 1 p.p.m. and 19 g of fish consumed/day."

The Total Diet Study indicates that overall PCB daily intake "is on the order of 5-10 mcg/day for the general population," the group noted, adding that this figure would not be applicable "to diets which include a high consumption of fish from certain areas with high PCB residues."

A study conducted under FDA contract recently showed that a group of sports fishermen consumed an average of 24-25 pounds of fish per person a year, with the highest individual exposure for a two-year period reported as 180 pounds per year, the report said. PCB residues in cooked fish from the contaminated areas were reported at from 0.36 p.p.m. to 5.38 p.p.m.

The group said there was a correlation "between the reported quantity of Lake Michigan fish consumed and the concentration of PCB in the blood of study participants, with the higher reported fish consumption being associated with higher PCB blood levels." The blood levels ranged from 0.007 p.p.m. in a control group to a high of 0.366 p.p.m. in the exposed group.

The investigators calculated that those in the exposed group annually ingested an average of 46.5 mg of PCB, with the range from 14.17 to 114.31 mg. "While no systematic adverse health effects could be demonstrated in the exposed group when

compared to controls, the investigators caution that any long-term chronic effects are unknown at the present time," the report said.

The subcommittee predicted "that exposure similar to those reported in this special group will continue and there is the likelihood that as sportsfishing becomes more popular, larger numbers of people may be exposed in a similar way."

Noting that exposure to PCBs from air and water is "probably minimal," the group said that adverse health effects have resulted from occupational exposure and from ingestion of contaminated rice oil in Japan. Noting the clinical effects found after the 1968 Japanese incident, the report said an epidemiologic study indicated that "the average cumulative intake of PCBs leading to overt symptoms was 2,000 mg, with the lowest dose leading to overt symptoms being 500 mg."

The subcommittee noted that it has been reported that the rice oil in Japan also contained chlorinated dibenzofurans at 5 p.p.m.

Turning to PBBs, the report said there is no evidence of acute health effects from exposure, but that "any chronic effects remain largely unknown." "A large scale epidemiological study is expected to get underway shortly to identify all the farm family members from quarantined farms; a large group of study subjects secondarily exposed to PBB through the purchase of farm products on a regular basis from quarantined farms, and a control group of individuals not exposed to PBB contamination," the group said.

Meanwhile, the report added, "a ten-fold safety factor for PBBs when compared to PCBs appears both reasonable and acceptable based on all currently available scientific data."

The HEW group made the following "general recommendations:"

"More complete and additional metabolism studies with various individual PCBs and PBBs should be undertaken. Attention to the formation of possible toxic metabolites of these compounds should be considered, as well as detecting and quantifying any specific biochemical parameters which may be affected as a result of such exposures. Based on the above, lifetime feeding studies should be conducted with selected commercial PCBs and PBBs mixtures, as well as selected individual PCBs and PBBs.

"Why some species seem to be more susceptible to the toxic effects of PCBs, and which are most closely related to man in their response should be determined. In addition, more experimental data is needed for the occupational PCBs settings; i.e., via the respiratory or dermal route. Additional toxicological evaluation should be made of fish and other foods which contain high levels of environmentally accumulated PCBs and other contaminants. Appropriate toxicological studies should be undertaken with PBBs in order to be able to make some predictions on possible human effects.

"The quantitative evaluation of halogenated biphenyl exposure to man with respect to blood and body fat levels, and any possible health effects, need further study. With

respect to PCBs, this may be accomplished by identifying a population of individuals consuming large amounts of fish contaminated with high levels of PCBs. In addition, those exposed industrially should be included in these efforts. With respect to PBBs, appropriate studies should be initiated with Michigan farm families exposed through consumption of contaminated meat and dairy products.

"Individual chemical components of PCB residues should be qualitatively identified and procedures for improving quantitation of these should be investigated. Commercial PCB (and PBB) mixtures need to be analyzed further to determine which chlorinated dibenzofurans (or, in the case of PBBs, whether any brominated dibenzofurans) are present as contaminants. Specific chlorinated dibenzofuran compounds must be synthesized for use in development of analytical procedures and to aid in identification of contaminants. Analytical procedures are needed to permit examination of foods for presence of chlorinated dibenzofurans and brominated dibenzofurans."

More specifically, the group recommended that fish eaters who are consuming substantial amounts of fresh water fish with high levels of PCBs be "followed prospectively with adequate dietary histories, blood and body fat levels of PCBs, a health questionnaire, liver function tests and other biochemical studies."

For PBBs, the report said those with high exposure, those with secondary exposure, and the control group should be "followed to assess any short and long term adverse health effects related to PBB exposure." Subgroups of the farm families from quarantined farms, the report said, should be studied by: (1) repeat PBB blood levels (2) matched blood-body fat PBB levels; (3) pregnant female-infant studies; and (4) a battery of biochemical studies.

The report said that "since induction of the mixed-function oxidase (MFO) enzymes may result in increased hormone metabolism or carcinogenic activation, exposure to the PCBs and PBBs should be limited on that basis alone."

The subcommittee explained that on a molar basis, PBBs are "approximately five-fold more potent than the PCBs in inducing increased levels of the (hepatic) MFO enzymes ..." Among the PCBs, the group said, it appears that potency increases with increasing chlorination. Also, the report said many commercial PCB formulations contain trace amounts of chlorinated dibenzofurans. "These compounds may be up to 170 times more potent as MFO inducers than the PCBs," the group said.

PCBs and PBB administered at 50 p.p.m. or higher in the diet to laboratory animals have caused porphyria, thyroid dysfunction, enzyme inhibition, changes in liver to body weight ratios, liver disorders, alteration in the level or utilization of vitamins A, D, and E, and of corticosteroids, the report said.

Some less chlorinated PCBs have also been shown to have a mild estrogenic effect in the immature rat and mouse, the group said.

The report said, however, that most of these effects "have not been studied in sensitive species or demonstrated at low exposure levels in laboratory animals."

Data suggest that PCBs and PBBs containing six or fewer halogen atoms are readily absorbed from the gut of higher animals, and that PCBs are not excreted to a great extent prior to metabolism, the report said. PBB metabolism studies have not yet been completed.

Those PCBs which are most readily metabolized and excreted, the report said, are most likely to be metabolized via arene oxide intermediates. It continued: "And whereas the reactivity of arene oxides varies greatly and often ultimately determines the toxicity, mutagenicity, or carcinogenicity of the parent compound . . . , the PCBs offer such a range of degree and position of substitution that it would not be unlikely to find that one or more of these PCB metabolites would have the proper stability to be a mutagen or carcinogen. Thus a move from the more highly chlorinated PCB formulations to the less chlorinated ones may help solve the long-term residues problem only to intensify other problems."

In animals, different commercial mixtures of PCBs "elicit different toxic responses in animals, and . . . different animal species vary in their susceptibility to the toxic effects of PCBs," the report said, noting effects in various species on reproduction, hepatic porphyria, and liver dysfunctions. In the mouse, liver tumors have been produced with some PCB products, the group noted.

If PBB toxic effects are similar to those of PCBs, the group recommended that, "at least in some species such as mink and monkey, long term low level exposure should result in measureable toxicity."

A "major part" in determining human exposure to PCB residues in food, the report said, "is evaluating the adequacy of the analytical methodology used and the significance of the data obtained."

Members of the HEW panel represented FDA, the National Cancer Institute, the Center for Disease Control, the National Institute for Environmental Health Sciences, and the National Institute for Occupational Safety and Health. Consultants to the panel represented the Environmental Protection Agency, Oak Ridge National Laboratory, the Agriculture Department, the Commerce Department, the National Marine Fisheries Service, and the Consumer Product Safety Commission.

CSPI URGES LEGISLATION TO HALT FDA'S "REVOLVING DOOR"

The Center for Science in the Public Interest is pushing for legislation which would bar Food and Drug Administration staffers from leaving and taking industry jobs for "several years."

CSPI noted in a news release that it is pushing for Congressional hearings to look into the so-called revolving door involving FDA.

In an article in the August issue of the group's Nutrition Action publication, Patricia Hausman called for legislation providing a "cooling-off" period, saying: