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Answering letter date

Subject FDA News Release

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FDA often uses Food Chemical News to quickly disseminate information. Note on Page 5 there is mention of a proposed interim order with a limit of 10 ppm in rigid plastic, 1 ppm in plasticized film, and an extraction limit of 50 ppb. If this issues as a proposal, there will be time for comment before it becomes final, either 30 or 90 days. I have an appointment with FDA for April 19 on the vinyl latex terpolymer and I was told that the vinyl chloride monomer order will have issued before then.

W. B. Ackart

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Attachment

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FDA REGULATION OF INDIRECT ADDITIVES TO BE REAPPRAISED

The Food and Drug Administration is embarking upon a reappraisal of the basic "assumptions" that underlie its regulation of indirect additives, it was disclosed at a March 25 meeting of the agency's National Food Advisory Committee.

The new look at indirect additives -- particularly packaging materials -- was prompted by: (1) unexpected migration problems with acrylonitrile-styrene-butadiene plastic bottles for soft drinks, which may delay use of plastic pop bottles for som time; and (2) possible vinyl chloride monomer migration into food products from rigid polyvinyl chloride containers (See FOOD CHEMICAL NEWS, March 18, Page 23)

Packaging Laboratory Established in Bureau of Foods

Richard Ronk, who is director of food and color additive work in the Bureau of Foods, disclosed that the Bureau has established a Packaging Laboratory to provide guidance in determining whether the system FDA has used for years in regulating indirect additives is satisfactory.

Ronk said that if the present "assumptions" do not prove out, FDA will have to develop a new method of evaluating indirect additives. If, however, the reappraisal indicates that there is no problem, "there are things we shouldn't be doing," he said.

The FDA-er explained that if there are no problems, the agency is spending too much time and money regulating indirect additives, such as adhesives components. "We're not convinced that the system doesn't work," Ronk stressed.

Bureau of Foods Director Dr. Virgil O. Wodicka, confessing to long-term "concern" about indirect additives, said no hazard has been known so far "because of the extent of our ignorance." He commented that this is true despite the fact that the United States has more stringent regulation of indirect additives than any other nation.

Wodicka said, "... There are still many problems ... and many decisions to be made."

Saying that indirect additives comprise "a very complicated area," Ronk said regulation of more than 10,000 indirect additives has been based on "a series of

assumptions." For example, he said FDA has relied on use of food-simulating solvents -- distilled water, 3% acetic acid, aqueous ethyl alcohol up to 50%, and heptane. The agency has required extraction in these solvents at 120° F. until equilibrium is reached.

Another assumption, Ronk said, was that the total diet consists of 80% aqueous food, 5% acid food, 5% alcoholic food, and 10% fatty food. "In its time, this was a good system," the FDA-er said, announcing the intention to reappraise the assumptions. However, he noted that there are problems with equilibrium studies, since migration has been detected long after equilibrium was believed to have been reached.

Noting the possible need to "evolve a system," Ronk said that if migrants have to be determined in foods rather than in food-simulating solvents, it will be a "fantastic analytical job."

Wodicka suggested that some of the unexpected migrants found after the equilibrium has been reached might result from de-polymerization on aging.

Wodicka said that he has regarded the review of "generally recognized as safe" substances as an "administrative tidying up of the files," because he expected few problems to arise. However, he expressed doubt about indirect additives, because of the nature of the "foreign" substances and lack of knowledge as to whether the human body possesses enzymes to handle them.

The Bureau Chief added that there is a possibility that a no-effect level modified by a safety factor may be "scientifically naive" in evaluating indirect additives. Wodicka said that FDA is now considering a way to review approved indirect additives.

Acrylonitrile Extractives Found After Six Months

Making the first public disclosure of the acrylonitrile problem, Ronk said that extractables have been found after six months, despite a much earlier equilibrium. Noting that the firm involved will bring in more data, he said that if there is extraction long after equilibrium was thought to be reached, "all of this will have to be held in abeyance." He said a no-effect level of .5 p.p.m. doesn't leave a sufficient margin of safety. Tests by the company indicated residues from migration ranged from 0.3 to 0.5 p.p.m., under the most severe conditions of the study.

Ronk noted the significant economic impact, saying that a number of firms are working on acrylonitrile bottles for soft drinks. He said one clearance has been granted on a Food Additive Petition filed by Standard Oil of Ohio. All of the companies have been notified of the need for new tests on migration, and there is some belief that new work may near completion by one of the six firms considering marketing acrylonitrile bottles.

The FDA-er hailed the acrylonitrile bottle as a "breakthrough in technology," but discussed the residue problem, including possible cyanide residues. Ronk concluded, "I'm sure they will solve the problem."

Interim Food Additive Order for PVC Would Set Limits

Regarding the PVC problem, Ronk said an "interim" Food Additive Order might be proposed to limit vinyl chloride to less than 10 p.p.m. in rigid plastic, with a limit in an end test of 50 p.p.b. For PVC films, the limit would be 1 p.p.m. in the film, with an end test limit of 50 p.p.b. The FDA-er said that if all of the vinyl chloride monomer migrated, the total would be less than 50 p.p.b. He also indicated FDA may require establishment of a no-effect level.

Wodicka noted that no interim Order proposal has yet been reviewed at the top levels of his agency.

Ronk reviewed tests made on PVC extracted in heptane for organotin stabilizers, saying it was "too bad" researchers did not look for vinyl chloride monomer at the same time.

He said there was a "significant amount of extractives" of organotin stabilizer, and that a small amount of the stabilizer -- 0.06 p.p.m. -- was still extracting after 14 months in cottonseed oil at 135° F. Ronk indicated this may be predictive of vinyl chloride monomer extraction.

The FDA official said a 1971 Italian study using inhalation indicated that vinyl chloride might be a carcinogen, noting that another Italian study is now underway attempting to reproduce the 1971 results. Carcinogenicity has not been established through ingestion, Wodicka noted.

Statistical Model Could be Used For Methods For Carcinogen

If vinyl chloride proves to be a carcinogen; Ronk said, methodology will have to be developed. Wodicka said the problem would then be one of enforcing "zero." He indicated that, if it were necessary, FDA might use the Mantel-Bryant statistical model, or some variation of it, to determine the needed sensitivity of method to demonstrate no residues of a carcinogen.

FDA proposed adoption of a variation of the Mantel-Bryant method for feed additives, and it was indicated last week that it might be applied to the controversial case of diethylstilbestrol (See story, Page 6)..

Ronk said British data indicate that vinyl chloride can migrate to a fatty food, and that it was also shown to migrate to an aqueous fruit drink. He added that any PVC problem is probably limited to "rigid formulations," and noted that the Society of the Plastics Industry has indicated that migration can be reduced through use of new formulations. He added that in the Italian test, 250 p.p.m. was reported as the lowest no-effect level.

Wodicka raised the question of FDA authority to regulate a finished formulation, noting that the agency has authority to regulate ingredients (food additives). Ronk replied that FDA can prescribe safe conditions of use.

The Bureau Director noted that FDA's limit of polychlorinated biphenyls in paper and paperboard has been stayed, and that the agency's authority to regulate paper has been questioned (See FOOD CHEMICAL NEWS, Feb. 11, Page 22). Wodicka said the outcome of the PCB matter may affect FDA's position on PVC containers.

Ronk predicted that FDA will be "more aggressive" in regulating indirect additives as a result of the knocking out of the old "housewares exemption" (See FOOD CHEMICAL NEWS, Dec. 3, Page 3).

He disclosed that FDA's long-pending proposal to issue a Food Additive Order for synthetic organic colorants in paper and paperboard (See FOOD CHEMICAL NEWS, July 12, 1972, Page 18) has gone back to the drawing board. He said the agency has found that the end-test specified in the proposal does not work. Ronk commented that FDA is now "back to ground zero" on the colorants proposal, and will probably have to work out a listing of approved colorants.

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MANTEL-BRYAN APPROACH MAY BE APPLIED TO DES METHOD

The Food and Drug Administration will ask an ad hoc adivsory group of experts to study the sensitivity of analytical method which would be needed for the continued marketing of diethylstilbestrol.

The deliberations of the group will be based on FDA's controversial proposal under which the sensitivity of analytical methods for carcinogenic animal drugs and other feed additives may be extrapolated from the results of toxicity studies (See FOOD CHEMICAL NEWS, July 23, Page 22). The FDA proposal is a variation of the Mantel-Bryan statistical model.

The question of the needed sensitivity of a method for DES became especially pertinent last week with the March 27 FDA proposal to revoke the official status of currently-used methods, as expected (See FOOD CHEMICAL NEWS, March 25, Page 19). At the same time, FDA urged use of a 14-day withdrawal period rather than a 7-day withdrawal period for DES-medicated feed.

Under the Delaney anti-cancer clause, as it applies to veterinary drugs, a carcinogen may be used only if no residues are left in human food when tested by an officially-approved analytical method. The proposal last week to revoke the official status of the mouse uterine method would leave DES with no place to go in a regulatory sense.

Recommendation by the ad hoc group of a required sensitivity of method would prepare the groundwork for adoption of a new official method which could retain use of DES.

Plans for the ad hoc committee and use of the Mantel-Bryan approach was disclosed March 26 at a meeting of FDA's National Food Advisory Committee by Dr. C. D. Van Houweling, director of FDA's Bureau of Veterinary Medicine. He said he