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February 28, 1978

To: All Members of:

SPI-/PVC Mailing List
Plastic Bottle Institute
Plastic Beverage Container Group
AN Safety Group
PET Safety Group
Food, Drug and Cosmetic Packaging
Materials Committee
PVC Safety Group

Letter Highlights

(1) An informal conference was held on February 24, 1978, with Sherwin Gardner, Deputy Commissioner for Food and Drugs. Mr. Gardner was cautiously optimistic that a way may be found to permit PVC packaging in particular, and plastics packaging in general to "live" in the shadow of the AN Beverage Container Decision.

(2) The need for assessments of risk due to exposure to low levels of VCM and PVC packaging was discussed. FDA's desire for completed chronic oral toxicology reports was also stressed by Mr. Gardner.

(3) Mr. Gardner urged that work should be done on the risk assessment approach as applied to other packaging systems, food-stuffs and other socially accepted activi-

ties; the ultimate idea would be to perhaps compare such assessments with VCM risk calculations.

(4) General principles (and problems) regarding the regulation of packaging materials were discussed. The need for a means, but even more so, for a palatable way to explain the wisdom of ignoring minute quantities of inconsequential migrants was accented, as well as the need to assure that attention is focused on those substances that truly require regulation.

(5) Mr. Gardner urged that industry act as promptly as possible to supply needed information along these various lines that might be useful to FDA.

Ladies and Gentlemen:

After I had a very interesting person-to-person meeting with Dick Ronk*/ on February 21, we followed up with a pre-scheduled February 24, informal conference in the office of Sherwin Gardner, Deputy Commissioner for Food and Drugs. The purpose of both sessions was to discuss problems and explore possible approaches to a solution of the situation that exists with regard to food packaging materials in general, and plastics packaging materials in particular in the aftermath of the Food and Drug Administration's (FDA) Acrylonitrile Copolymer Decision. Present at the conference in addition to Mr. Gardner were Margaret Gilhooley, Assistant to the Chief Counsel for FDA, Dr. Daniel Dixler of our office, and myself.

To summarize what was a relatively free-wheeling conversation to the degree possible, Mr. Gardner offered his opinion that the AN Decision does leave what he called "wiggle room," provided some special attention is given to combining appropriate risk assessments with scientific

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*/ Richard Ronk is the Director of the Division of Food and Color Additives of FDA's Bureau of Foods.

evidence that might show that extrapolation of migration as a result of the presence in packages of high levels of substances to extremely low levels is invalid.

As a means of loosely structuring the wide ranging discussion, five topics (questions), suggested by members of the Bureau of Foods staff were used. For the sake of specificity, the questions were set with PVC as a frame of reference, but it is evident that the same principles are applicable to all other packaging materials.

The first topic concerned the desirability of obtaining data on "time to appearance" of animal tumors. To do this, complete animal toxicological studies on VCM, as well as an update on epidemiological studies are needed. These can provide a basis for risk analysis. Gardner suggested that risk analyses should not be restricted to Mantel-Bryan extrapolations but that other procedures such as those based on linear models utilizing one-hit and multi-hit postulates should be used as well.

Mr. Gardner pointed out that FDA has no completed chronic oral toxicity tests of VCM in its files. Absent these and updated epidemiology, FDA feels that risk assessments will not be sufficiently convincing, especially to the lay public subjected to whatever might be said by vocal consumer activists. Furthermore, without adequate completed study results, additional "safety factors" will have to be built in to any risk assessments to compensate for the lack of data; these safety factors are so "conservative" they almost always act to make the risk at any exposure level appear to be far higher than would be calculated from more complete data.

In addition to the dose-related incidence of tumors in the animals fed at high VCM levels, good measurements of "time to tumor" development as related to dosage would be most helpful. There is much evidence that the time to development of chemically induced tumors is dose-dependent. Therefore, it may be possible to show that the time required for the development of tumors as a result of very low exposures will far exceed a human lifetime. This would provide a somewhat different and additionally supportive basis for more favorable risk assessment.

In light of the need, it was agreed by all present that every effort should be made to obtain final reports on the chronic toxicity of vinyl chloride in order to provide a firm factual basis for the various assessments.

Attention was then directed to the desirability of comparing the risk associated with exposure to low or "non-detectable" levels of vinyl chloride with the risks associated with other types of packaging and other socially accepted risks as well. Here in particular, the comparison of the risk calculated for exposure (if any) to vinyl chloride by way of packaging should be compared with the risk assessments FDA is developing for aflatoxin in nuts and cereal grains, and lead from canned foods. In this connection, Mr. Gardner stated that the risk assessments on aflatoxin and lead (the aflatoxin assessment can be expected to appear in the Federal Register within a few weeks, the lead document is still in preparation) should provide important new reference points.

In addition, risk assessments for saccharin, and, where available, risk assessments published by other Federal agencies should be utilized. Mention was made of the National Cancer Institute's "Risk Assessment for Exposure to Chloroform in Drinking Water," which was utilized by the Environmental Protection Agency (EPA) in its recently Proposed Interim Primary Drinking Water Regulation relating to the control of organic chemical contaminants in drinking water. (43 Fed. Reg. 5755, February 9, 1978.)

The need for validated analytical methods for the determination of residual vinyl chloride in PVC products was discussed very briefly. The procedure developed by FDA (and distributed by us to the entire PVC mailing list) is believed to be among the most sensitive procedures available. Nevertheless, FDA is requesting of the VCM/PVC industry that those who have more sensitive procedures, or those who can provide confirmation of the FDA procedure, file appropriate reports with the Hearing Clerk.

Mr. Gardner seconded a suggestion made to me by Mr. Ronk that a paper be prepared and submitted to the Hearing Clerk to explain in lay language what a "monomer" is, how it is used to prepare a polymer or resin, and how residual monomer is removed from the polymer, or finished plastic. Mr. Gardner confirmed that there are many in FDA who do not clearly understand this subject, basic as it may seem to us.

The last point that was discussed related to a statement of suggested principles on how to regulate packaging materials. It is now recognized, especially with the general availability of more sensitive analytical procedures, that extremely minute amounts of a large variety of substances (derived from impurities in starting materials, by-products of polymerization, and the like) may be detectable in packaging materials. Since some migration, no matter how small, can be postulated (if the AN Decision doctrine were applied) for each of these substances, the regulation of food additives would become a practical impossibility if a toxicological study of each of these postulated trace migrants was required. Thus, some balance must be reached so that regulatory attention can be directed, properly, to migrants which require such attention because of their quantity, use or inherent toxicity. The others should properly be ignored because the quantity and extent of their use or toxicological nature make attention unnecessary. We pointed out that we had proposed such an approach in our SPI Petition (7CP3313-Docket No. 77P-0122)and Mr. Gardner responded by saying that it seemed unwise to set any absolute figure without regard to the nature of the possible migrant. In fact, this concern is addressed in our Petition.

In discussing regulatory principles, we speculated that residual monomers might be dealt with as unavoidable contaminants (subject to tolerances) since they were not added to the plastics and could not be completely removed under good manufacturing practices. This approach could lessen some of the burdens which could be imposed by FDA's latest interpretations of the applicability of the Food Additives Amendment to monomers and other polymerization chemicals. Mr. Gardner stated his belief that FDA would not "buy" this concept because of a long history of dealing with monomer residues as food additives, but I think it would be premature to consider this avenue completely closed.

The conference ended on a cordial note with all agreeing that the exchange of ideas was mutually helpful.

Based upon the comments and suggestions made by Messrs. Ronk and Gardner, a prompt "action" agenda would seem desirable. Our immediate "shopping list" in this respect is as follows:

(1) Every effort should be made to obtain final reports from the various chronic oral toxicity studies on VCM which have been completed or which are nearing comple-

tion. In this connection, we understand that at least three such studies have been undertaken: by Professor C. Maltoni in Italy, BIBRA in England, and CIVO-TNO in Holland. Each were reported to be utilizing a different mode of the administration of the VCM, its volatility posing a major problem in administration of measured dosages.

An early report from the CIVO-TNO study had been submitted to FDA shortly after the study began, but we have heard nothing further. We heard over a year ago that the Maltoni study was ended and the pathology was well under way. Nevertheless, we are unaware of any final report on this work. As for the BIBRA study, we know nothing other than that it was reported to have been started.

(2) Risk assessments for exposure to VCM in packaging, for exposure to other packaging materials, and for other activities should be undertaken. Mantel-Bryan, linear "one-hit," linear "multi-hit," and other extrapolation procedures should be explored.

(3) The FDA request for comments on analytical methodology for RVCM, should be accomodated. This can probably best be done by individual companies, but an SPI response might be considered.

(4) A clarifying paper for a lay audience on "What is a Monomer, and How it Grows" should be prepared for submission to the Hearing Clerk.