JOSEPH E. KELLER
JEROME H HECKMAN
CHARLES M. MEEHAN
WILLIAM H. BORGHESANI, JR.
ROBERT R. TIERNAN
WAYNE V. BLA
DAVID L. HILL
MARTIN W BERCOVICI
EDWIN B. SPIEVACK
PETER M. NEMKOV
JOSEPH E. HADLEY
CAROLE C. HARRIS
WILLIAM W PUGH

LAW OFFICES
KELLER AND HECKMAN
1150 17TH STREET, N. W.
SUITE 1000
WASHINGTON, D. C. 20036

TELEPHONE
202 296-2100
CABLE ADDRESS "KELMAN"

March 5, 1974

M. S. J.
MAR 14 1974

Mr. Richard J. Ronk
Director, Division of Food
and Color Additives
Room 5825, HFF-330
Food and Drug Administration
200 C Street, S.W.
Washington, D.C. 20204

Re: Prior Sanctioned Polyvinyl Chloride (PVC) Resin; Proposed Rule Making, 38 Fed. Reg. 12931 (May 17, 1973)

Dear Mr. Ronk:

On December 20, 1973 a conference was held between FDA personnel and representatives of the Society of the Plastics Industry, Inc. (SPI). At that conference SPI was advised of data which was considered necessary by the Food and Drug Administration before a final decision could be made concerning the subject proposal. A copy of a summary report of that meeting dated February 5, 1974 was filed with the Hearing Clerk. Another meeting is now scheduled between representatives of the Food and Drug Administration and SPI on March 8, 1974 to inform the Food and Drug Administration of the steps now underway to supply the requested data; this communication is intended to provide, in a preliminary fashion, some of the information to the Food and Drug Administration in advance of that meeting so that the conference itself can be more productive.

For ease of reference, this letter follows the questions set forth in the aforementioned February 5th summary.

Toxicology

The first item that was discussed at the December 20, 1973 conference concerned toxicological matters relative to polyvinyl chloride. It was requested that an extensive review of the literature concerning the toxicology of polyvinyl chloride be conducted and that a treatise be prepared concerning the applicability of the "Viola Study" and inhalation data to the use of polyvinyl chloride as packaging materials. The Society of the Plastics Industry has authorized Food and Drug Research Laboratories of East Orange, New Jersey, a highly regarded research laboratory well known to the Food and Drug Administration, to prepare such a treatise.

In addition and more significantly, SPI has authorized the same laboratory to prepare a protocol for a feeding study with rats designed to assess the toxicological potential, if any, of vinyl chloride monomer when administered by ingestion at levels reasonably related to possible dietary intake, but significantly exaggerated to provide an adequate intensification of effects. The sensitivity of the analytical procedure (50 ppb) already submitted to the Food and Drug Administration in connection with the proposed rule making provides a base point for the feeding study.

The Food and Drug Administration is well aware that a controlled feeding study using vinyl chloride monomer presents very serious problems in manipulation. The extreme volatility of the monomer makes it very difficult to administer controlled known levels of the vinyl chloride monomer, especially to animals like rats that nibble all day long.

In order to solve this problem the SPI Ad Hoc Committee appointed a Task Force to consider all aspects of the problem. The possibility of encapsulating either the monomer or a liquid food containing moderately large quantities of monomer in microcapsules whose walls permit

controlled permeability of the vinyl chloride monomer was carefully considered. While this approach was deemed to be potentially possible, the consensus of the expert Task Force set up by SPI was that the development of such an encapsulation procedure would present a major research problem in itself.

The possibility of administering controlled quantities of monomer by freezing was also considered. The difficulties in maintaining the food at a temperature below the monomer freezing point (approximately -14° C), and yet making it readily available to the animals all day long seemed to pose significant manipulative difficulties; thus, this possible procedure was also discarded.

Administration of a test diet by gavage is a well established technique, and was considered in this case too. This approach is certainly feasible, but known difficulties associated with the procedure made the Task Force reluctant to recommend it. In particular, the trauma experienced by the animals complicates whatever experimental responses might be noted. Secondly, an entire day's exposure is generally administered in one or two large doses, each of which is at a significantly higher concentration than would be the case if the entire day's quantity were administered equally distributed throughout the entire diet. The possibility of side effects due to the excessive concentration (and not due to the total dosage) must be considered as introducing the possibility of an undesirable experimental confusion.

Vinyl monomer is reported to be significantly soluble in edible oils so the possibility of administering oil containing vinyl chloride monomer was considered. It was found, however, that vinyl chloride monomer evaporated very rapidly from such oil. It would, therefore, be extremely difficult to administer significant and known quantities of vinyl chloride throughout the day by such a means. Furthermore, in light of the rat's known intolerance to larger

quantities of oil in its diet, the possibility of introducing complications into the program by use of excessive quantities of oil ruled against this approach.

After considering a number of other possible alternatives, the Task Force recommended that the following two possible experimental procedures be investigated:

1. Administration of vinyl chloride monomer absorbed on activated carbon.

2. The use of vinyl chloride-containing water in a closed system.

It is known that some activated carbons will absorb and hold vinyl chloride monomer with relatively little evaporative loss. It was considered likely that if carbons of different absorptive powers were tested, a suitable carbon could be found that would hold appropriate quantities of the monomer to permit administration as part of the diet and yet would release the monomer at an adequate and controllable rate in the animal's gut. The use of this procedure would have to be supplemented by adequate analytical work to assure that the intended level of vinyl monomer was actually being administered to the rats.

It is also known that vinyl monomer can be dissolved in water to a limited extent. If this water were used in a closed system, it may well be possible to administer known quantities of VCM to rats and measure, reasonably accurately, the quantity of vinyl monomer that the rats ingest. The possible loss of monomer at the exposed tip of the "sipping tube" would require assessment and control; but this approach also seems to be a feasible one.

We are submitting a draft protocol which includes the experimental evaluation of both these procedures. It will be noted that it is intended to use radio-tagged monomer

during the exploratory phase in order to provide an analytical assessment of the bio-availability of the monomer. After a suitable procedure for administering the test diet has been established, the protocol continues in the conventional fashion for the feeding of vinyl monomer. This protocol is being submitted as a discussion draft. The recommendation of the Food and Drug Administration are hereby solicited.

Analytical Procedures

The second item discussed at the December 20, 1973 meeting concerned the analytical procedures supplied by M & T Chemical Company and Continental Can Company. The possibility of combining a mass spectrograph with a gas chromatograph as a means of confirming that a suspected chromatographic peak was vinyl chloride monomer was considered carefully.

A 5 microliter sample containing 50 ppb of VCM would contain a total quantity of vinyl chloride of 0.25 nanograms (5×10^{-6} liter $\times$ 50 $\times$ 10^{-9} = 250 $\times$ 10^{-15} liter). We have been advised by mass spectrographers that this quantity of vinyl chloride is below the detection sensitivity limits of most mass spectrographs. A confirmatory procedure can probably be developed using larger sample sizes to provide larger quantities of vinyl chloride for the mass spectrograph.

Rather than utilize a mass spectrograph which is not available to many laboratories, the analysts of the companies concerned have proposed that (a), a gas chromatograph method utilizing an electron capture detector may be useful as a means of providing confirmation that a given peak detected by the "standard" flame ionization detector is indeed vinyl chloride, or more preferably, (b) that any suspected sample be additionally analyzed using two more columns with significantly different retention times for vinyl chloride. If all three columns show a response at the known vinyl chloride retention times, then it may be confidentaly concluded that the substance detected is indeed vinyl chloride.

An acceptable procedure for handling samples suspected of containing vinyl chloride is being written and circulated. It will be submitted promptly.

Additional Extraction Data

It was requested that equilibrium extraction tests on the new polyvinyl chloride compounds using other food simulating solvents in addition to ethyl alcohol be conducted with water, dilute acetic acid, and Wesson Oil at 120° F for periods of time ranging from 20-30 days. It has been found that those new polyvinyl chloride compounds that yielded no detectable vinyl chloride monomer to 50% ethanol likewise yielded no detectable vinyl chloride monomer to the additional test solvents. Chromatograms have been requested and will be supplied promptly.

It was also requested that data be provided involving longer storage periods to show a relationship of vinyl chloride monomer migration from the new polyvinyl chloride formulations as a function of time with 50% ethanol and edible oils. These tests have now been started by a number of different laboratories and data will be supplied when they become available.

Procedure for Residual VCM in Compounds

It was requested that a method be provided for the determination of vinyl chloride monomer in polyvinyl chloride resin and/or compound. The analytical procedures already provided are suitable for that purpose. However, the samples of PVC should be dissolved in tetrahydrofuran (THF) (approximately 5%) in a closed container to minimize loss of VCM, and the resultant solution used as the sample. The injection of these large quantities of polyvinyl chloride tends to foul the column and a prepacking of glass wool is recommended. Because of the complications introduced by the presence of polyvinyl chloride, the procedure is not as sensitive as when applied to extraction solvents. Nevertheless, it is reported to be sensitive to approximately 5-10 ppm of residual vinyl chloride monomer in polyvinyl chloride resin or compound.

Manufacturing Processes

It was also requested that a description of the new manufacturing process for PVC resin and/or compound be provided. Each individual manufacturer of PVC compound has developed its own procedures and considers the details of their processes to be proprietary trade secrets. In general, it can be stated that the preparation of polyvinyl chloride compound with low residual vinyl chloride monomer involves the proper application of time, temperature, and the removal of volatilized monomer.

In order to provide the Food and Drug Administration, however, with specific information regarding each individual manufacturer's process, it was suggested that each manufacturer set up a confidential master file with the Food and Drug Administration. The manufacturing details and quality control procedures can then be set forth by each manufacturer, subject to the assurance that this information will be kept confidential as a trade secret. SPI suggests that if FDA feels such information is required, a requirement for the submission of master files might be included in the final rule making.

Use of Regrind

It was requested that data be supplied showing the VCM content of PVC bottles made from a 50% blend of virgin compound with 50% regrind. The data shown in Table I are available on "new" type compounds made by three different manufacturers, and "old" compound made by one manufacturer.

Japanese Bottle Compounds

Data was requested on the Japanese manufacturers' PVC compounds including a description of the resin and compound preparation as well as VCM levels. This information is, in general, not available since such information is

usually kept confidential as a trade secret. However, one of the Japanese manufacturers has revealed that it prepares its bottle compound by making a dry blend using an intensive mixer. During this operation heat is applied and a vacuum is drawn. [This is also believed to be true of some American manufacturers].

This same Japanese manufacturer has stated that its bottle compounds have less than 1 ppm of residual VCM. The analysis is believed to have been conducted by dissolving the plastic sample in THF, precipitating the dissolved polymer with methanol, and analyzing the resultant supernatant liquid by the Association of Official Analytical Chemists (AOAC) gas chromatographic procedure. Since no validation data is available, the reliability of this procedure cannot be judged.

Can Enamels, and Cap Liners and Gaskets

The Food and Drug Administration required more definitive information concerning the possibility of migration of vinyl chloride monomer from cans and bottles which have coatings and plastisols containing polyvinyl chloride; specifically, more information on the nature of the resins and processes used.

The can coatings based on polyvinyl chloride are applied from solutions of the resin in volatile solvents. In the first place, many of the resins used for can coatings are made by solution polymerization, whereas resins used to make rigid compounds for bottles are generally made by the suspension process. The solution-made resin is recovered from the solvent in an extremely fine form so that if any residual monomer were entrained by the polymer, the enormous surface-to-volume ratio would provide ample opportunity for the residual monomer to be removed during the drying operation. Furthermore, the actual recovery step whereby the resin is removed from the solution tends to eliminate entrappment of vinyl monomer so that even before drying there is essentially no monomer entrained within the polymer particles. In confirmation of these expectations, it has

been reported by the major manufacturer of solution-made resins for coating purposes that its entire line of such resins shows no detectable residual monomer using a gas chromatographic procedure that is claimed to be sensitive to approximately 1-5 ppm.

Vinyl gaskets and cap liners are made by the plastisol technique. As is well known, this technique involves the preparation of a stable dispersion of partially solvated resin in plasticizer that contains other necessary formulating additives. For technological reasons it is necessary that the dispersion remain stable with respect to solids content and viscosity for a long enough period of time to permit the reasonable storage of such dispersions. Furthermore, modern technology requires that the plastisol resins be of the "stir-in" type so that the dispersion can be prepared without the use of expensive grinding equipment.

For these reasons, essentially all the plastisol resin used is made by spray drying to provide a product of extremely small particle size and without agglomerates that cannot be easily broken up. The spray drying procedure encourages the complete removal of monomer. Further, as was true in the case of the can coating resins, the large surface-to-volume ratio for the plastisol resins facilitates the evaporation of such residual monomer as might otherwise be entrained in the resin of large particle size.

During the preparation of polyvinyl chloride bottles, the compound which contains essentially no plasticizer is generally melted in an enclosed system as in the barrel of an extruder. The very viscous melt is then extruded as a rather thick-walled tube which is very rapidly enclosed in a mold in which the bottle is blown and chilled. Because of the viscosity of the melt, the short exposure time to the atmosphere and the relatively low ratio of exposed surface to volume of plastic, the resulting bottles can contain entrapped vinyl chloride monomer if the bottle compound contains such monomer.

In the case of the plastisol processing or the preparation of can coatings, the resin is diluted with very significant quantities of solvent or plasticizer. Frequently, plastisols will contain in the range of 50 parts of plasticizer per 100 parts of resin or even more; and the coating solution will almost never contain more than 50% of resin, and often contains less. Consequently, when these products are heated in order to fuse the resin in the case of the plastisol, or evaporate the solvent in the case of the can coatings, ample opportunity is provided for the evaporation of any traces of residual monomer that might conceivably remain in the resin. This is so because the systems contain large amounts of solvent or plasticizer permitting easy volatilization of any VCM, because they are heated to high temperatures, and because they are exposed to the atmosphere for significant time periods.

In order to test the hypothesis that the drying of can coating solutions would effectively eliminate any residual vinyl monomer, suspension resins of varying molecular weights, particle size, and porosity were prepared by one manufacturer. Homopolymers, and 15% vinyl acetate copolymer were included in the study. The residual monomer level in these specially prepared resins ranged from 100 - 3,000 ppm of vinyl chloride. These resins with known vinyl chloride monomer levels were put into solvent solutions in typical can enamel formulations, were cast into films, and baked under commercial conditions. The dried films were then tested for residual vinyl chloride monomer; no VCM could be found in any baked film using a test procedure sensitive to approximately 2 ppm in the polymer.

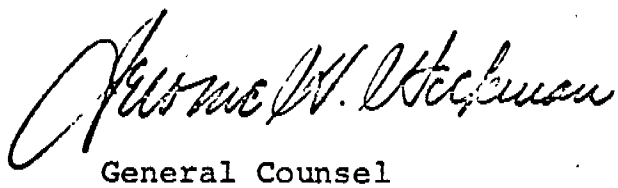
This same manufacturer also reported that its major plastisol grade polymers showed no detectable vinyl chloride monomer when commercial material was sampled from warehouse stocks.

We hope the foregoing information is adequate to permit the Food and Drug Administration Staff members to prepare for the planned conference. We believe it is

apparent that the various manufacturers are moving diligently and responsibly to assure that the polyvinyl chloride products they provide will pose no problems to consumers when used in food contact use, and to provide the Food and Drug Administration with all the information that it will require in order to reach a decision in the proposed rule making procedure.

It is recognized that additional data has been promised to the Food and Drug Administration; this will be submitted as soon as it can be accumulated by scientifically sound procedures which have been carefully conducted. In the meantime, however, if any questions remain or if there is any further information that the Food and Drug Administration requires, we will be happy to respond as fully and as accurately as we can.

Cordially yours,



General Counsel
The Society of the Plastics Industry, Inc.

Of Counsel:

Keller and Heckman
1150 Seventeenth Street, N.W.
Washington, D.C. 20036
Telephone: 296-2700

TABLE I

Residual VCM in Bottle Walls

Manufacturer	Compound Type	Sample Type	Residual VCM in Bottle Walls, ppm
A	new	virgin bottle	n.d. (<10)
		50% regrind bottle	n.d.
B	new	virgin bottle	n.d.
		50% regrind bottle	n.d.
C	new	virgin bottle	n.d.
		50% regrind bottle	n.d.
D	old	virgin bottle	67
		50% regrind bottle	58