BIO-MEDICAL RESEARCH
DOCUMENT DESCRIPTION FORM

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Source (Journal, Vol., Number, Pages, Date)

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The Food and Drug Administration and the Vinyl Chloride Problem—An Overview

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Recent evidence has shown that chronic exposure to vinyl chloride by inhalation may cause cancer in laboratory animals and in man. Its possible oral effects are currently being investigated. The history of the significant events leading to the investigation of this chemical is presented. The current and future activities of the Food and Drug Administration in this area are also described.

The formation of polyvinyl chloride (PVC) from vinyl chloride (VC) was first observed by Liebig in 1835, but it was not until the 1930's that industrial production was achieved in the United States. VC is produced at an annual rate of 5.3 billion pounds in the United States, and trails only polyethylene and polystyrene in total volume. A substantial portion of this production goes into PVC and various copolymers which are used to make articles or components of articles for food contact use. These include food packaging materials, coatings and parts for food processing equipment, flexible tubing, and water pipe. VC polymers are also used as packaging materials for drug products, blood, cosmetics, and shampoo, and as components of medical devices. These packaging uses accounted for more than 300 million pounds of PVC in 1973. Until recently VC was also used as a propellant in some aerosol preparations.

Prior to the enactment of the 1958 Food Additives Amendment to the Federal Food, Drug, and Cosmetic Act, sanctions or approvals were granted for the use of certain substances as packaging materials for foods. These substances were not considered food additives when used for this purpose, as long as they were of good commercial grade, were suitable for association with food, were used in accordance with good manufacturing practice, and did not migrate into the food contained within. In 1951 and 1956, Dr. A. J. Lehman, then Chief of the Division of Pharmacology of the Food and Drug Administration (FDA), wrote articles concerning food packaging in monographs published by the Association of Food and Drug Officials of the United States. Dr. Lehman listed various resins which were considered acceptable for use as food contact surfaces. These sanctions or approvals were based on the understanding that the resins were insoluble in food-simulating solvents. PVC was included in the listing based on available analytical data which indicated no migration of the resin to food under conditions of use. The Lehman articles and FDA acceptance of these uses for PVC formed the basis for the prior sanction of this resin, and in most instances, subsequent regulations providing for the safe use of PVC and VC copolymers in food contact articles have relied on this approval. Thus, the overwhelming majority of the food additive petiti[ons] relating to the use of VC polymers contain[ed] analytical data concerning the migration of the VC monomer. Additionally, the presence of VC in food was thought to be highly unlikely, since it is a gas.

In 1968, the Bureau of Alcohol, Tobacco and Firearms authorized the experimental bottling of distilled spirits in PVC bottles. In early 1973, Schenley Distillers noted significant organoleptic differences between various alcoholic beverages packaged in PVC and in glass. The cause of these differences was investigated, and Schenley determined that VC was the causative agent. Their findings of 10–20 ppm free VC in liquors were subsequently confirmed by FDA scientists. In May 1973, FDA issued a notice of proposed rulemaking for "prior sanctioned" PVC resin. The proposal defined the identity of this plastic, and excluded its use in contact with alcoholic foods because of the known migration of VC.

In December 1973, FDA met with representatives of the Society of Plastics Industries (SPI) to discuss the details of the toxicological and chemical information required for a final decision on the proposed rulemaking. As a result, SPI obtained information relevant to the use of

Received August 16, 1974.

This paper was presented at the 88th Annual Meeting of the AOAC, Oct. 14–17, 1974, at Washington, DC.

PVC, including the analysis of various foods for VC. Their findings showed that VC also migrated into nonalcoholic foods.

Up to that time, there was no information indicating that VC was carcinogenic. In January 1974, however, a PVC resin manufacturer announced that 3 workers at one of its plants had died of angiosarcoma of the liver (a rare form of liver cancer) since 1971. Subsequent announcements of deaths attributed to this rare disease were made by other industrial concerns, both here and abroad.

In a February 1974 meeting sponsored by the Occupational Safety and Health Administration (OSHA), Dr. Maltoni of the Institute of Oncology (Bologna, Italy) discussed preliminary results of his investigations on VC. He found angiosarcoma of the liver and other types of tumors in rats at levels as low as 250 ppm by inhalation. (Earlier, in 1971, Dr. Viola of the Regina Elena Institute for Cancer Research (Rome, Italy) had reported tumor formations in rats exposed to very high VC levels, but these findings were for the most part ignored.)

Because of the widespread use of VC polymers and copolymers, the Commissioner of the FDA formed an inter-bureau task force to coordinate FDA's activities on the VC problem, and meetings were subsequently held internally and with industry representatives. In April 1974, FDA sent out about 4400 letters to manufacturers of drugs and aerosol products requesting the recall of products using VC as a propellant. Soon after, 9 companies voluntarily recalled a total of 91 different products, mainly comprising cosmetics and drugs. Their use was also effectively banned through an FDA *Federal Register* proposal.

Later, OSHA published an emergency standard of 50 ppm for employee exposure to VC, and shortly thereafter, issued a proposal which would establish a permanent standard of "no" VC detected using methodology capable of determining 1 ppm. OSHA subsequently proposed the banning of any household product containing VC.

The Environmental Protection Agency (EPA) was also quite active. The agency banned the use of VC as a propellant in pesticide aerosol preparations, and conducted a survey of VC levels outside several industrial plant sites. It was their opinion that the data indicated that there was no imminent hazard to people living near the plants examined. Although various levels of VC were found in the plant effluents, no evidence was obtained to indicate that the chemical was present in detectable levels in drinking water. At about this same time, Professor Maltoni, in a joint New York Academy of Sciences-American Cancer Society meeting, disclosed a finding of 1 liver angiosarcoma in rats at a level of 50 ppm by inhalation, in addition to several other types of tumors.

In June 1974, the first known cases of angiosarcoma in plant workers in the PVC fabricating industry were reported. This industry produces the articles of commerce such as upholstery, floor tiles, and phonograph records. These 2 cases were later confirmed by the National Cancer Institute.

After the removal of products containing VC monomer propellant in food, drug, and cosmetic products from the market, FDA turned its attention to the leaching or migration of VC from packaging materials made of PVC. These include containers for foods, blood, biologics, and drugs, and PVC water pipes.

FDA has held many meetings with industry in which the manufacturing and processing of PVC polymers has been discussed. Industry is cooperating and is submitting data to FDA on VC levels throughout various stages of manufacture. Their information indicates that residual VC levels in PVC vary greatly, depending on the polymerization process, compounding, and subsequent processing used. Four main processes are used to make PVC resin, and each of these tends to produce a different particle size and porosity of the basic resin. The degree of entrapment of VC monomer varies accordingly. In addition, the drying method can also differ, and this results in the removal of varying amounts of VC. The basic resin may contain levels of anywhere from several ppm to 2000 ppm, depending on the process used, and the final plastic product may contain anywhere from several hundred to much less than 1 ppm.

To date, VC has been shown to be carcinogenic by inhalation only, and it is not as yet known whether it can cause angiosarcoma or other malignant tumors by ingestion. Work directed toward answering these questions is underway by several investigators, and FDA is awaiting the results of these experiments. Should

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VC prove to be carcinogenic orally, it would be automatically regulated by the Delaney amendment to the Federal Food, Drug, and Cosmetic Act. This would mean that no measurable level of VC would be permitted in foods consumed by humans.

Our present information indicates that highly plasticized and/or thin films of PVC contain extremely low levels, if any, of monomer. The blood bag is an example of highly plasticized PVC, and analyses conducted by both FDA and industry have thus far failed to reveal the presence of VC in this product. It appears that the plasticizer enables residual monomer to easily diffuse out of the plastic during processing. In the case of thin films such as those used in meat wrap, several factors probably account for the low residual monomer content. These include plasticization, thermal history during processing, and the fact that the monomer need migrate only a very short distance to escape the plastic.

The vinyl industry is working intensively on the VC problem, and it is expected that worker exposure, emissions, and residual monomer in the plastic will eventually all be reduced to levels that are considered safe.

FDA is presently actively engaged in the development of analytical methodology for the detection and quantification of VC in PVC and in foods packaged in PVC. To date, preliminary results indicate that VC may be quantitatively determined at levels of 50 ppb or lower in vegetable oil and food-simulating solvents representing aqueous, acidic, alcoholic, and fatty foods, and at levels of 1 ppm or lower in the PVC plastic itself. Much of our progress to date has resulted from an excellent cooperative effort between FDA and the PVC industry. The details of our analytical work are described in the following paper.

The agency will continue to work vigorously on the VC problem in an effort to ensure the safety of PVC in foods and other products regulated by FDA.