Occidental Chemical Corporation
PVC Products

Robert D. Luss
Group Counsel

July 23, 1986

Peter L. de la Cruz, Esq.
Keller & Heckman
1150 17th St., N.W.
Washington, DC 20036

Dear Peter:

RE: **OSHA Regulation of PVC Resins and Compounds**

I have just returned from vacation and have read your summary of the July 11 meeting at OSHA. I would have hoped that it went better but I still am confident that our position is correct. I have attached a report prepared by our Toxicologist concerning PVC and the IARC study. This report should be included in your next reply to OSHA. Please keep me informed on this matter and if you need any additional information, feel free to contact me.

Sincerely yours,

RDL/rm

Attachment

cc: Dr. R. Gottesman

Occidental Chemical Corporation
Environment, Health & Safety

MEMO

R. D. L.

JUL 15 1986

TO: R. Luss, Esq DATE: July 11, 1986

FROM: P. E. Gurba PE Gurba

SUBJECT: Presumed Carcinogenicity of Implanted Polyvinyl Chloride

cc: H.F. Dubec, D.A. Guthrie

Summary

Polyvinyl Chloride (PVC) is not an animal carcinogen, and available epidemiological data is insufficient to classify PVC as a human carcinogen. Even though results of rodent tests of implanted PVC indicate that a local sarcoma (not carcinoma) can be formed under defined conditions, NO implantation site sarcoma or carcinoma has been observed in humans who have received similar plastic implants.

Test conditions employed to examine PVC carcinogenicity in animals has found that a large variety of materials other than PVC can produce implantation site sarcomas. When the test conditions were carefully examined, it became apparent that natural materials (e.g. glass, silk, gold, and other metals) as well as synthetic materials could all elicit the same reaction. Examination of a larger body of information than cited in the IARC monograph on PVC leads one to conclude that implantation per se rather than the PVC material was responsible for the increased incidence of rodent sarcomas.

Finally, a wide variety of the synthetic materials which produced implantation site sarcomas in rodents have been approved by the Food and Drug Administration (FDA) for permanent implantation into humans or contact with food materials used by humans. This experience with human populations which

covers nearly 40 years of experience has not found any increase in any type of tumors associated with the implants.

Background

The International Agency for Research on Cancer (IARC) in its volume on: "Some Monomers, Plastics and Synthetic Elastomers, and Acrolein" (Volume 19) has NOT classified PVC or vinyl chloride-vinyl acetate copolymers as carcinogens (1). In their summary of experimental data (p. 417) IARC indicated that both materials produced local sarcomas (i.e. at the site of implantation). It was also pointed out that when PVC was implanted, the incidence of sarcomas varied with the size and form of the implant.

Sarcomas are a type of highly malignant tumor made up of material that resembles embryonic connective tissue. These types of tumors in humans often metastasize (spread to other tissues and organs) very rapidly and fatally. By contrast to the response in humans, implantation site sarcomas appear to remain localized, and they often develop slowly. This indicates that the rodent response may not be a reliable predictor of how humans will respond to an implanted foreign body.

The production of a local (implantation) site sarcoma in rodents (mice and rats) is recognized to be a common occurrence for many materials. IARC has provided information on the production of implantation site sarcomas for a variety of materials which is also found in the same Volume 19. In contrast to rodents, other animals and humans do not appear to respond to foreign bodies by producing a local sarcoma.

It is the contention of some researchers that "...in humans, no tumor, benign or malignant, has ever been observed to develop in the tissues that were in direct physical contact with surgically implanted synthetic organic material in any location." (15). Also, work has been done with other animals which indicates that it is only rodents which seem to develop implantation

site sarcomas (11,16,18,19).

It will become evident from some of the studies summarized below that many materials besides PVC cause the implantation site sarcoma response in rodents whether synthetic or natural. Available human experience with these same implanted materials, however, does not show the same response as rodents.

Caprolactam polymers (Nylon 6) have been approved by FDA for food packaging, and there is widespread use for consumer products such as clothing. When caprolactam polymers were implanted into rats, however, local sarcomas were found in four out six animals at the end of the test period (2). When this was later examined by other researchers, it was found that local sarcomas could be produced from nylon disks but not from powdered nylon.

Polyethylene (PE) in both its low density (LDPE) and high density (HDPE) form are used widely for and have FDA approval for use in consumer packaging of food, infant clothing, and toys. PE is also widely used for biomedical applications such as facial reconstruction, oral surgery, replacement of bones in the ear, joint protheses, intra-uterine devices, and other surgical procedures.

When PE materials were examined in rodent carcinogenicity assays, they produced local sarcomas in mice (3,4,5) and rats (4,6). Tumors (sarcomas) were produced by a variety of different shaped and formed material, and it was found that the actual occurrence of tumors was very dependent upon shape (4,6). In addition to shape, surface characteristics were important, and it was found that local sarcomas developed with greater frequency with smooth surfaced disks compared to those with a rough surface (5).

In a number of the experiments examining PE carcinogenicity, glass was used as a control material which was expected to be inert. In a series of experiments done by Oppenheimer (7), the incidence of implantation site sarcomas produced by glass was equal to or greater than the incidence of these

tumors produced by PE. In another experiment performed by Lavorgna (8), rats were implanted either with glass or various plastic discs, and only the sites with implanted glass disks developed tumors.

As with PE it was found that glass had to have a specified form in order to produce a local sarcoma. Powdered glass was found to be generally ineffective in producing a response, but the incidence could be increased dramatically if smooth, glass disks were implanted (12,13,14). Glass fibers could also produce the same effect, and the frequency of the response depended upon the ratio of length to diameter of the fibers (17).

Polytetrafluoroethylene (teflon) is another important polymer which has FDA approval for use in biomedical devices such as bone replacement, vascular repair, and heart valves. When implanted into mice (9,10) or rats (11), local sarcomas developed. In control animals implanted with glass, some animals developed tumors (10), but others were tumor free (11). Since the form of the glass implants was not specified in the last study, previous discussion would lead to the conclusion that the glass was powdered.

Silicone rubber compounds are the last materials that will be discussed even though many other materials show the same pattern. This family of materials have produced the typical local site sarcoma in rodents after implantation whether disks/buttons (13) or slabs, balls or or squares (20) were implanted. In contrast to the positive rodent responses, the experience with human use of these materials is quite different.

Silicone rubber compounds have been used extensively in reconstructive surgery for humans as well as augmentation mammaplasty. In the case of augmentation mammaplasty, over 3100 women were examined, and no increase in breast cancer could be detected (21). A similar study could find no physiological or pathological changes in human breast tissue related to silicone rubber implants.

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