BIO-MEDICAL RESEARCH
DOCUMENT DESCRIPTION FORM

Duplicate in all cards: →

63 68	69 76	77 78
1980	0000319	VC
year as-1961-	File number [Right justify [Numeric only]	Sub-Index Code

R&S 111300

Author(s), as Last Name FS (No Punctuation) and coden for journal as JAMA preceeded by one blank space

1 20	21 40	41 60	61 62
VAN BSCH, GJ	VAN LOBTON, MJ		11
			12
			13

Title of Report; end with space-hyphen-hyphen-space. Follow with Index Terms, separated from each other with comma-space. Avoid other punctuation; do not abbreviate.

1 2	61 62
Vinyl Chloride: A Report for European Assessment	21
	22
	23
	24

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

1 2	61 62
TOXICOLOGY 4, 1-4 (1975)	31
	32

Brief Summary

1 2 10	61 62
SUMMARY:	61
	62
	63
	64

0000319

Toxicology, 4 (1975) 1—4
© Elsevier/North-Holland, Amsterdam — Printed in The Netherlands

VINYL CHLORIDE: A REPORT OF A EUROPEAN ASSESSMENT*

G.J. VAN ESCH and M.J. VAN LOGTEN
National Institute of Public Health, Bilthoven (The Netherlands)

(Received August 5th, 1974)

R&S 111301

During 1973, increasing concern was expressed about the possible carcinogenic and other effects of vinyl chloride. The practical implications include the health of industrial operatives exposed to vinyl chloride during the manufacture and processing of PVC. The presence of vinyl chloride in PVC has been unequivocally demonstrated, as has its ability to migrate into food and drink packaged in PVC containers. The migration of vinyl chloride into the atmosphere from PVC is also a strongly presumed, though less documented, probability.

On 26 March 1974, a group of European toxicologists discussed the available toxicological and migration data on vinyl chloride, with special reference to its carcinogenic potential. The meeting was held at The National Institute of Public Health, Bilthoven (The Netherlands). The participants were Dr. Böhme (Federal Republic of Germany), Dr. Carstensen (Denmark), Dr. Crampton (U.K.), Professor Gatti (Italy), Dr. Kroes and Dr. van Logten (The Netherlands), Professor Schlatter (Switzerland) and Professor Truhaut (France), with Dr. van Esch acting as Chairman.

The essential points of the toxicity and carcinogenicity of vinyl chloride known so far may be summarized as follows:

(*1*) Inhalation studies with animals show positive carcinogenic effects. In 1971, Viola et al. (Cancer Res., 31 (1971) 516) reported tumours of the skin, lungs and bones in rats exposed to a high vinyl chloride concentration (30 000 ppm) in the air for 4 h daily on 5 days/week for 12 months. The skin tumours arose in the para-auricular region. Reports of further studies carried out in Bologna, Italy (Chem. Eng. News, 25 February (1974) 16) confirm the carcinogenic response and some results are shown in Table I. These results were obtained in Sprague-Dawley rats exposed to the stated concentration of vinyl chloride in the inspired air for 4 h daily on 5 days/week over a period of 12 months. In addition to the angiosarcomas indicated

* This report has already appeared in the BIBRA Bulletin for June 1974 (Vol. 13, No. 5) and is reproduced here because of its general and topical interest with the permission of Dr. R.F. Crampton, Director of the British Industrial Biological Research Association (BIBRA), Woodmansterne Road, Carshalton, Surrey, SM5 4DS (Great Britain).

em, in any
out permissic

TABLE I

CARCINOGENIC RESPONSE IN RATS EXPOSED TO VINYL CHLORIDE IN THE INSPIRED AIR

Exposure level (ppm)	Rats with liver angiosarcoma	Number of rats exposed
10 000	6	69
6 000	21	72
2 500	9	74
500	7	67
250	2	67
50	0	64

in Table I, some rats also developed zymbal-gland tumours and nephroblastomas. In concurrent studies, exposure of rats to vinyl acetate at levels up to 2500 ppm was not followed by the appearance of any tumours.

(2) There are strong indications that vinyl chloride exposure results in liver tumours in man. A number of cases of angiosarcoma of the liver have been reported in the United States in operatives exposed to vinyl chloride. This tumour is very rare in man. It is possible that the initial cases recorded will be followed by the appearance of others, and comment on this possibility has already been made by the Center for Disease Control, U.S. Department of Health, Education and Welfare.

In addition to the possible carcinogenic response in man, vinyl chloride exposure has been associated with the clinical syndrome, acroosteolysis. Full descriptions of the signs and symptoms and clinical findings of this condition have been published (Dinman et al., Arch. Environ. Hlth., 22 (1971) 61; Harris and Adams, Brit. Med. J., 3 (1967) 712; Jühr et al., Deut. Med. Wschr., 97 (1973) 2034; Lange et al., Intern. Arch. Arbeitsmed., 32 (1974) 1).

(3) Other effects in man have also been recorded (Kramer and Mutchler, Am. Ind. Hyg. Ass. J., 33 (1972) 19). In individuals occupationally exposed to concentrations in the air varying from 10 to 300 ppm over periods up to 25 years, indications of liver dysfunction have been observed. This particular effect has not been confirmed in animals, in that inhalation of vinyl chloride by dogs, rabbits and guinea-pigs over a period of 4—6 months has not produced any signs of liver disturbance (Torkelson et al., Am. Ind. Hyg. Ass. J., 22 (1961) 354).

The relationship between the chemical structure of vinyl chloride and its toxicological effects was discussed. A large number of compounds contain double bonds which may lead to free radical formation. These include styrene, acrylic acid, acrylonitrile, acrylates, vinylidene chloride, vinyl acetate and safrole, a substituted allyl benzene known to have carcinogenic properties in experimental animals. The absence of a carcinogenic response to vinyl acetate indicates that other factors affect its biological activity. Therefore,

R&S 111302

the reactivity of vinyl chloride with other compounds in the environment and in food and its metabolic route in the body are of considerable importance. Little information on these points is available; for instance, no data exist to indicate the degree, if any, to which vinyl chloride may act as an alkylating agent.

The factors that affect the migration of vinyl chloride from PVC were discussed. In January 1973 the Food and Drug Administration began to receive reports of possible stability problems with PVC bottles used for distilled spirits. The level of vinyl chloride migrating varied, with some samples in a high range of 10—20 ppm. As there were no prior indications that contact between PVC and food would result in migration of monomer, the figure of 10—20 ppm was astonishingly high.

Some data were available for migration into non-alcoholic beverages, food and other materials. It is not possible to include all the basic data, but the following will indicate the order of magnitude of migration. From PVC in which vinyl chloride was present at a level of 30 ppm, migration into water, soft drinks and blood (after 40 days) produced concentrations of 0.02—0.05, 0.0002 and 0.014—0.08 ppm respectively.

The extent of migration depends on the initial content of vinyl chloride in PVC, and this can vary greatly. Thus, in PVC bottles, the content of vinyl chloride may be as low as 5 ppm and as high as 400 ppm (and up to 800 ppm in PVC film). Migration also depends upon time of storage, as illustrated by a sample of beer which contained 2 ppm vinyl chloride after 6 years in PVC bottles containing 70 ppm.

Other factors that might influence migration are the type of industrial process used, the effects of additives to PVC formulations and conditions of usage. It is known that information on these and other aspects has been generated by industry, and the need for a round-table discussion with industry was agreed by all participants.

On the basis of available migration data, an estimate was made that less than 100 μg vinyl chloride is the likely oral daily intake by man (in Europe). However, further data are needed to quantitate this, and consideration should also be given to compounds formed by the interaction of vinyl chloride with the chemical constituents of food and drink, on which no data were available.

The following conclusions were reached and agreed unanimously.

(*1*) Industrial exposure to vinyl chloride is the most important problem. Full epidemiological data, including detailed clinical records of operatives with tumours or other alleged effects, should be reviewed. The no-effect level of 50 ppm in inspired air indicated by Professor C. Maltoni is too high to adopt as a Threshold Limit Value*. Present levels of industrial exposure

* After the meeting it was learned through personal communication that 50 ppm vinyl chloride in inspired air is also carcinogenic to rats. This indicates the need for further evaluation, as soon as results of the oral studies on vinyl chloride become available.

R&S 111303

should be reduced as far as possible. Environmental considerations should include the atmospheric effluent from industrial plants. Of particular importance is the elimination of hazard to the operatives from exposure to high levels of vinyl chloride during the cleaning of polymerization vessels.

(2) Methods for reducing the residual vinyl chloride in plastic products to very low levels should be explored urgently. This is of particular importance where PVC is used for food and drink containers and wrappings.

(3) At the present time there is no need to recommend that PVC should be banned as a food-wrapping material, provided active steps are taken as indicated above. The basis of this conclusion is that relatively high concentrations of vinyl chloride (by inhalation) are needed to produce a carcinogenic effect. In comparison, the exposure of man from food intake is probably much lower. The further quantitation of this factor will be possible when oral studies on vinyl chloride have been completed. Furthermore, it was noted that even less toxicological data were available on possible alternative plastics for food wrappings. It was thought desirable and possible that PVC used for food and drink packaging should contain less than 20 ppm vinyl chloride monomer. In effect this represents the establishment of a food grade of PVC, to ensure very low levels of contamination.

(4) The current situation is that the problem of vinyl chloride has been broadly defined. Its final solution depends upon the evaluation of further data, such as: (*a*) Epidemiological studies in man concerning vinyl chloride-linked diseases. (*b*) Levels of industrial and environmental exposure. (*c*) Effects of oral dosing of vinyl chloride in animals. (*d*) Investigations on whether the induction of liver tumours by vinyl chloride is preceded by liver dysfunction and cirrhosis, as can be found with selenium, or whether it behaves like nitrosamines, with which no cirrhosis of the liver is observed. (*e*) Metabolism of vinyl chloride, including alkylation studies. (*f*) Percutaneous migration of vinyl chloride. (*g*) Levels of vinyl chloride in food; estimated daily intake in children and adults. (*h*) Interaction of vinylchloride with food and drink components. (*i*) Levels of vinyl chloride in PVC products (sheets, film). (*j*) Levels of vinyl chloride in potable water and PVC tubing.

The vinyl chloride problem should be capable of solution without recourse to total abolition of PVC manufacture and usage, but it was recognized that the latter policy might be adopted in some countries as a matter of expediency. Should this occur, there would be considerable risk to other plastics materials. It is obviously desirable that the co-operation of all interested parties be attained to facilitate and expedite the resolution of this problem.