CHEMICAL MANUFACTURERS ASSOCIATION

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September 20, 1984

Comment Clerk
Criteria and Standards Division
Office of Drinking Water (WH-550)
Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460

Dear Comment Clerk:

Comments of the Ethylene Dichloride Program Panel of the Chemical Manufacturers Association on EPA's Proposed National Primary Drinking Water Standards (49 Federal Register 24330, June 12, 1984) are enclosed. Please call Dr. Shah of my staff at 202/887-1192, if you need additional information.

Sincerely,

Geraldine V. Cox

COMMENTS OF THE
CMA ETHYLENE DICHLORIDE PROGRAM PANEL
ON EPA'S PROPOSED RECOMMENDED MAXIMUM
CONTAMINANT LEVELS FOR VOLATILE
SYNTHETIC ORGANIC CHEMICALS
IN DRINKING WATER

CMA

COMMENTS OF THE CMA ETHYLENE DICHLORIDE PROGRAM PANEL ON EPA'S PROPOSED RECOMMENDED MAXIMUM CONTAMINANT LEVELS FOR VOLATILE SYNTHETIC ORGANIC CHEMICALS IN DRINKING WATER

National Primary Drinking Water Regulations; Volatile Synthetic Organic Chemicals: Notice of Proposed Rulemaking, 49 Federal Register 24330 (June 12, 1984)	)

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EXECUTIVE SUMMARY

The Ethylene Dichloride (EDC) Panel of the Chemical Manufacturers Association ("CMA") submits these comments on the proposed rulemaking which would establish a recommended maximum contaminant level (RMCL) for ethylene dichloride, as published at 49 Fed. Reg. 24330, June 12, 1984. The EDC Panel represents all U.S. manufacturers of EDC and most manufacturers of vinyl chloride, which is derived from EDC. The EDC Panel has reviewed the Draft Criteria Document for 1,2-Dichloroethane, February 1984 and the document, Occurrence of 1, 2-Dichloroethane in Drinking Water, Food, and Air, November 18, 1983. The Panel's comments address both the criteria and the occurrence documents as well as the proposed rulemaking.

The Panel finds that both documents contain serious deficiencies. As a result, they do not support the EPA's proposed establishment of a RMCL for EDC. The EDC Panel also finds that treatment of data in the occurrence document leads to erroneous conclusions regarding the presence of EDC in drinking water and, in turn, its ingestion by the public. Review of the occurrence document indicates that the extrapolation of data from the Federal survey of surface water systems to a nation-wide projection of contamination is faulty. The projected national occurrence for EDC indicates that the chemical will be present in certain size water systems even though there is no evidence of such contamination in the survey data. Furthermore, the Panel finds that there are serious discrepancies between the combined criteria and occurrence documents and the EPA's Draft Health Assessment Document for Ethylene Dichloride, April 1984, (HAD). While the draft HAD has deficiencies, the final HAD should be the scientific data base on which the EPA should rely in its regulatory activities.

The Agency's assertion that EDC is a mutagen as well as an animal carcinogen is based on an erroneous interpretation of the scientific data. EPA apparently has relied on the NCI gavage bioassay for its conclusion that EDC is a probable human carcinogen. The NCI bioassay on EDC, however, is seriously flawed. In addition, there are negative studies conducted by four independent researchers that do not even support the conclusion that EDC is an animal carcinogen. The weight of the evidence does not support EPA's contention that EDC is a probable human carcinogen.

I. COMMENTS ON DRAFT CRITERIA DOCUMENT

A. Undue Reliance on the Russian Literature

The criteria document relies inordinately on the Russian literature, which has been criticized as being deficient in experimental details and other scientific data. The criteria document extensively referenced the work of Vozovarya (1971, 1974, 1975, 1976, 1977). The HAD addressed these Russian studies as follows:

> However, it is difficult to evaluate or seriously consider these reports since they are presented with insufficient detail for critical scientific review. Inadequacies in these reports include: lack of original data, various techniques and test mentioned but results not presented, no information on the source of (or) purity of the chemical, statistical analysis mentioned, but the type of statistical tests not stated. (HAD, p 9-127).

Regarding the work of Urosova, the HAD states:

> The above comments apply similarity to the study by another Russian scientist, Urosova (1980), who reported that EDC accumulated in the milk of nursing mothers. This is obviously an important observation, however, it cannot be accepted as scientific evidence. This report was presented in a subjective, anecdotal manner with many inadequencies (sic) in reporting (p 9-128).

Moreover, in the NIOSH Technical Information Document,

> "An Analysis and Critique of Behavioral Toxicology in the USSR", the authors note "here and there throughout the text we explicitly criticized some elements of procedure or of processing and reporting data." and "As a result, most published reports provide little information about matters of experimental control or the procedures used." (p 2 and p 7 respectively).

Accordingly, EPA should delete, or reduce in emphasis, the many citations to the Russian literature in any future revisions of this criteria document.

B. Toxicity

The criteria document extensively delineates the acute toxic effects of EDC poisoning, primarily via ingestion by man or by inhalation in animals. The purpose of the current rulemaking is to establish an RMCL for EDC for drinking water, based on the long-term effects of the chemical. The levels of exposure cited in the acute toxicity discussions are many orders of magnitude greater than the highest level of EDC found in the federal water surveys. Accordingly, the acute toxicity data are not germane to the current proposal.

Regarding chronic toxicity in humans, the criteria document indicates that relatively few data are available, but it goes on to state that, "Chronic exposures to 1, 2-dichloroethane by inhalation or absorption usually result in progressive effects that closely resemble the effects described for acute exposure....". It is further stated that, "The concentration and exposure times associated with the onset of chronic symptoms in humans is (sic) difficult to

deduce from the existing literature." (p VI-3). The second statement would suggest that the data base for chronic human exposure is of a flimsy nature and this opinion is enhanced by the lack of literature references in support of the first statement. The criteria document continues by saying:

> The more subtle toxic effects which may result from chronic low level environmental exposure have not been reported. Of particular interest is the accumulation of 1, 2-dichloroethane in the body with chronic low level exposure....(p VI-4)

The lack of reports of "more subtle toxic effects" is undoubtedly due to the lack of such effects; traditional toxicology has long recognized the existence of a threshold, below which toxic effects are not present. The use of the term "accumulation" is misleading. While there may be a preferential tissue distribution during exposure, studies have shown EDC to be removed in a relatively short time after exposure ceases and bioconcentration or bio-accumulation does not occur. (Reitz et al, 1982)

C. Pharmacokinetics

In the HAD, 56 pages are used to discuss EDC pharmacokinetics, using the most recent data available. In the criteria document, there are only 14 pages discussing pharmacokinetics and, with the exception of perhaps two or three references, with the major emphasis placed on articles and data published prior to 1971.

While extensive pharmacokinetic data have been generated in rats and mice exposed to EDC by both inhalation and ingestion, neither of the major investigations (Spreafico et al, 1980; Reitz et al, 1982) were discussed or referenced in the criteria document. The results of these recent studies indicate that there is no bioaccumulation of EDC in test animals. Also we are not aware of any evidence of such occurrence in humans. The data also show that elimination kinetics for EDC are nonlinear, i.e., the metabolic pathways become saturated. Further, results from inhalation exposure are in accord with the dose-dependent pharmacokinetics exhibited after intravenous and oral dosing of EDC. They strongly indicate that the kinetics of absorption, distribution and elimination of EDC are appropriately described by nonlinear kinetics that takes into account saturable processes.

In the General Section (p III-2), it is stated that "Further research on the pharmacokinetics and metabolism of dichloroethane is strongly indicated, particularly with respect to low chronic exposures by inhalation or ingestion, if rational and intelligent assessment of the hazard potential of 1,2-DCE is to be made." When the Office of Drinking Water reviews the recent literature mentioned above, they must conclude that the studies to date are adequate to allow them to achieve their objectives.

The criteria document, in its discussion on metabolism, states:

> Some of the most significant questions to be answered deal with the possible toxic effects produced by metabolites of the haloalkanes on liver and kidney as well as their mutagenic, teratogenic and carcinogenic potential. (p III-5)

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EPA appears to be overlooking a major point that when testing is conducted on the whole animal, the chemical under investigation is being metabolized. Consequently the metabolites' toxic effects are being evaluated simultaneously with those of the parent compound. In other words, the toxic effects observed in whole animal testing are the sum of the effects attributable to the parent compound and its metabolites.

The criteria document also identifies four substances -- chloroacetaldhyde, chloroethanol, S-chloroethylglutathoine and S-chloroethylcysteine -- as strong mutagens in bacterial test systems. The document notes on p III-1 that these substances are "postulated" to be metabolites of EDC. In fact, however, these substances have not been isolated in EDC studies.

D. Mutagenicity

When metabolically activated, EDC is, at most, a very weak mutagen as acknowledged in the criteria document. (p III-1) The discussion of the mutagenicity test data in the criteria document should be more balanced. For example, the document presents the study of McCann et al (1975) as being positive, while the HAD describes this study as being "negative or at best only marginal positive." (p 9-134) In fact, induced revertants were only 25 above background. This is not significant; hence the results could not appropriately be considered even marginally positive.

The four assertedly positive studies on Drosophila melanogaster reported in the criteria document are inadequate to draw any firm conclusion as to the mutagenicity of EDC. Two were inadequately reported Russian studies (Rapoport, 1960; and Shakarnis, 1969) in which the purity of the EDC is apparently unknown. The third study by Nylander et al, 1978, showed a statistically significant increase in lethal recessive mutations, but the actual increase was only 1.73 percent over the untreated flies. This low percent increase above background casts doubt on the statistical analysis of the data. The fourth Drosophila study by King et al, 1979, was conducted for purposes of method development and should not be used to assess the mutagenicity of EDC.

The criteria document overlooks two cytogenetic studies of EDC which were negative (King et al, 1979; Jenssen and Ramel, 1980). Furthermore, host mediated assays were negative. Considering all the data on mutagenicity, EDC cannot be considered as more than a very weak mutagen in metabolically activated systems, and in vivo mutagenicity in mammals has not been shown. Several studies on reproduction and teratology have been conducted on rats, mice and rabbits and no teratogenic or reproductive effects were identified. (Alumont et al, 1976; Rao et al, 1980; and Lane et al, 1982)

E. Covalent Binding

The criteria document states, "There are several studies reported in the literature which demonstrate covalent binding of 1,2-dichloroethane to macromolecules, including DNA." (p V-41) Not covered in the subsequent discussion is the work of Reitz et al, 1982, who conducted DNA alkylation and binding studies in rats exposed to EDC by both inhalation and gavage. In

general, higher levels of DNA alkylation (three to five times) were seen after gavage as compared to inhalation exposure. No treatment-related lesions were observed in any of the animals studied by necropsy, clinical chemistry or microscopic examinations of tissues after single gavage (150 mg/kg) and inhalation (150 ppm, 6 hours) exposures, or after multiple (10) gavage exposures. Reitz et al, 1982, did not observe a relationship between DNA alkylation in the tissues studied and the purported susceptibility of these tissues to tumor formation. Lutz, 1979, suggested a classification for chemicals binding to DNA in vivo. According to his CBI (Chemical Binding Index), EDC would be rated as having very "weak" potential to produce genotoxic lesions in vivo. The CBI for EDC was calculated to be 3-12 nano mol chemical/-mol DNA at 1 nano mol/kg. For reference purposes, aflatoxin has a rating of "strong" with a CBI of 17,000; dimethylnitrosamine has a CBI of 6,000; and 2-acetylaminofluorene is rate "moderate" with a CBI of 560.

This perspective must be considered before making statements such as that on the bottom of page V-42, in reference to Banerjee's and Van Duuren's work: "These observations lend support to the hypothesis that a correlation exists between binding DNA and the compound-induced carcinogenicity."

F. Carcinogenicity

The current proposal would establish an RMCL for EDC on the basis that this chemical is a probable human carcinogen. The weight of the evidence does not support this conclusion which is based essentially on the bioassay conducted on rats and mice by Hazleton Laboratories for the National Cancer Institute (NCI). That study, as recognized in the draft criteria document, is difficult in a variety of respects. These deficiencies range from the potential of crosscontamination between the mice gavage studies being conducted on 17 other (mostly halogenated) chemicals in the same room; high and early mortality in both male and female rats; and the presence of chronic murine pneumonia in both rats and mice. Although not mentioned in the criteria document, there was also a problem of early mortality and low survival in both male and female mice. (NCI, 1978)

The problem of crosscontamination is addressed in the proceedings of the Banbury EDC conference, where Dr. H. B. Plotnick (1980) of NIOSH stated, "I won't challenge your results, but you have an awful lot of faith in a study that you consider not to be flawed and which I consider to be [so] utterly flawed that you can't rely upon it." Because of concerns that the NCI bioassay is not technically adequate and has not been quality assured, CMA requested and received permission from the National Toxicology Program (NTP) to conduct an in-depth audit of the study. This audit was undertaken the week of August 13, 1984, and an audit report will be submitted to the Agency.

The observation of tumors in the 1978 NCI gavage study is contradicted by the negative results obtained by Maltoni in a more recent inhalation bioassay on rats and mice. Although the criteria document does reference the Maltoni study, the document tends to discount Maltoni's findings by stating that "the negative results may be explained by the fact that Maltoni et al, did not follow NCI guidelines in the conduct of their study." (p V-26) It is very uncertain as to what this statement refers, but the Maltoni study was conducted at the maximum

tolerated dose. An analysis presented at the Banbury EDC Conference concluded that, "the two highest dose levels in the inhalation study were entirely comparable on a mg/kg/day basis to those yielding a strongly positive result in the NCI study." (Hooper et al, 1980)

In addition to the negative findings of Maltoni, the criteria document briefly describes the negative inhalation study by Spencer et al, 1951, and the negative pulmonary bioassay in Strain A mice by Theiss et al, 1977. We did not see any reference to the negative skin painting on ICR/Ha mice which was conducted by Van Duuren et al, 1979.

On the basis of the above studies, the EDC Panel does not believe that a convincing case has been established to show that EDC is a probable human carcinogen. The evaluation of the carcinogenicity of EDC must therefore be more balanced, with negative studies being given equal weight to the purportedly positive NCI study. Other scientists apparently share our opinion as reflected in their conclusion that "[a]dditional long-term oral ingestion studies employing several species of animals are needed to determine if DCE (EDC) is a carcinogen." (National Academy of Sciences, 1980) Moreover, we understand that NTP has recently decided, because of the major difference in response between dosing by gavage and dosing by inhalation, to conduct a multistrain rodent bioassay on EDC in drinking water or by microencapsulation if the drinking water route is not technically feasible.

For the foregoing reasons, EDC should not be treated as a carcinogen for purposes of developing a RMCL in this proceeding. Instead, as discussed hereafter, the RMCL should be based on a properly derived ADI for noncarcinogenic effect of EDC.

G. Human Exposure

It is interesting to note that this section of the criteria document is prefaced by the statement:

> Even in limiting the analysis to these three sources (drinking water, food, and air), it must be recognized that individual exposures will vary widely based on many personal choices and several factors over which there is little control. Where one lives, works, and travels, what one eats, and physiologic characteristics related to age, sex and health status can all profoundly affect daily exposure and intake. Individuals living in the same neighborhood or even in the same household can experience vastly different exposure patterns. (p IV-1)

With this declaration of uncertainty, the criteria document then delineates that 5.7 percent of the U.S. population serviced by public water supplies will be exposed to 0.5-5 ug/l or 0.5-5 ppb of EDC in drinking water, with the balance of the population being exposed to lower concentrations, if at all. (As discussed below, this estimate is overstated, since it is based on an unjustifiably high frequency of occurrence value.) This level of EDC is sufficiently low that until recently such concentrations were analytically unmeasurable. It is questionable whether existing laboratories could correctly and reproducibly measure EDC at this level on a consistent basis. Even if this

estimate is correct, this indicates that 94.3 percent of the population is exposed to less than 0.014 ug/kg/d, as compared to the criteria document's Acceptable Daily Intake ("ADI") for EDC of 7.45 ug/kg/d, based on noncarcinogenic toxicity. Even the 5.7 percent or 12,232,000 persons who are allegedly exposed to 0.5-5 ug/l or 0.014-0.14 ug/kg/d are exposed to 50-500 times less EDC than permitted by the ADI. In fact, based on the criteria document data, no one is actually exposed to the ADI in drinking water, e.g., the highest estimated exposure of 0.29-0.57 ug/kg/d (p IV-3) is still 13-26 times less than the ADI. Moreover, the value of the ADI, as established in the criteria document, is too low by a factor of 10. The safety factor for a NOEL based on a long-term animal study should be 100, not 1000. (NAS, 1977)

II. COMMENTS ON OCCURRENCE DOCUMENT

A. Exposure through Water Systems

Review of the occurrence document reveals inconsistencies in the treatment of data. The NORS surface water data shown in Table 15 indicate 22 positive systems, while the text indicates that for this survey, 16 of these "positive" systems were below the minimum quantifiable concentration ("MQC"). Reference to Appendix A of the occurrence document indicates that the MQC is the "level below which it cannot be determined whether a VOC is present and, if so, at what concentration." Accordingly Table 15 should indicate only 6 positive systems.

Based on our reading of the text, we found only 9 positive systems in 1059 groundwater supplies for an incidence of 0.8 percent. This is fairly close to the 9 positive systems in the 1001 ground water supplies as shown in Table 22, although it is unclear which groundwater sources were deleted as being duplicative. Nevertheless, the projected national occurrence of EDC in groundwater supplies indicates that 99.7 percent of groundwater sources contain either no EDC or only levels below 0.5 ug/l and that no groundwater supply would exceed 5 ug/l. Accordingly, it would appear that EDC in groundwater supplies presents a negligible risk to the public.

Regarding surface water supplies, the occurrence document is much less clear. After the correction to Table 15 and based on the text, Tables 15-21 indicate 11 positive sources, i.e., greater than 0.5 mg/l, out of 575 surface water sources, for an occurrence rate of 1.9 percent. Reference to Table 26 shows an entirely different picture. The 575 surface water sources have decreased to 301 while the number of positive sources, i.e., greater than 0.5 ug/l, has swelled from 11 to 18. The seven sources indicated as being less than 0.5 ug/l should not be included in Table 26 at all, since they are below the MQC. The projected national occurrence of EDC in surface water sources, as illustrated in Table 27 is irrational, with no basis in Tables 15-21. There were no incidents of contamination in system sizes 25-3,300 (see p 10), yet Table 27 shows 67 systems in this size category as containing 0.5-5 ug/l EDC and 67 surface water systems to contain 10-20 ug/l EDC. This is a totally unreasonable interpretation of data. It should be noted that in Table 27, the same numbers appear in the columns "0.05-5" and "10-20", up to a system size of 10,000. This would suggest an error in transposing data to the table or an incorrect model being used. The projected occurrence in surface water systems must be reevaluated as part of the current rulemaking. Accordingly, the

estimation that 12,232,000 persons (5.7%) will be exposed to drinking water containing 0.5-5 ug/1 EDC must be recalculated. Similarly, the estimates of 143,000 persons being exposed to greater than 5 ug/1 EDC must be redone.

B. Total Exposure

Assuming an air exposure of 0.49 ug/m^3 as might be found in an urban/suburban area and drinking water containing 0.5 ug/1 EDC, we can calculate the total daily exposure to both adults and infants.

	Adult	Infant
Water	0.014 ug/kg/d	0.12 ug/kg/d
Air	0.16 ug/kg/d	0.11 ug/kg/d
	0.174 ug/kg/d	0.23 ug/kg/d

These values of 0.17 ug/kg/d for the adult and 0.23 ug/kg/d for the infant are well below the ADI of 7.45 ug/kg/d. Even at a level of 5 ug/1 EDC in drinking water, the total daily intake is 0.30 ug/kg/d for the adult and 1.31 ug/kg/d for the infant, and still well below the ADI.

III. DEVELOPMENT OF RMCLS

The proposed rule indicates that in establishing a RMCL relative to a noncarcinogenic response, EPA is considering taking 20 percent of the ADI as the value for the RMCL. This is based on the assumption that 20 percent of an individual's exposure arises from drinking water. Accordingly, EPA would reduce the AADI for EDC by 80 percent from 0.260 mg/1 (7.45 ug/kg/d) to 0.052 mg/1 (1.49 ug/kg/d). Another approach would be to use the actual occurrence data in establishing an appropriate RMCL. We have shown above that the total daily combined intake from air and water is not likely to exceed 0.30 ug/kg/day or about 4% of the ADI. Taking the source dominated exposure, which will most likely be the worst case exposure, the daily intake from air would be only 1.6 ug/kg/day. Since the ADI for a non-carcinogenic response for EDC is 7.45 ug/kg/day, 5.85 ug/kg/day or 78% of the ADI is still available towards the intake of EDC in drinking water. Thus, it is apparent that the proposal to establish a RMCL at 20% of the AADI for EDC is unduly conservative; a RMCL value of up to 5.85 ug/kg/day (78% of the AADI would seem adequately protective of the public health.

IV. TOTAL VOCS

The current proposal requested comment on the establishment of RMCLs and MCLs for the total VOC content in drinking water. This subject was brought before the Science Advisory Board in December, 1983. The consensus of the SAB was that the concept of additivity had not been scientifically established and thus a RMCL or MCL for total VOC content was not warranted. Moreover, the National Drinking Water Advisory Council in its August 1984, meeting also

recommended against the adoption of RMCLs or MCLs for Total VOCs. The EDC Panel concurs with these opinions and is opposed to the establishment of RMCLs or MCLs for Total VOCs.

V. RMCLS FOR CARCINOGENS

The EDC Panel concurs with the National Drinking Water Advisory Council's opinion that RMCLs should not be zero. A more workable and responsible approach to setting RMCL's for carcinogens is described in the Comments of the Chemical Manufacturers Association which were submitted to the agency on September 10, 1984. We endorse the CMA position and urge that it be adopted.

FREQUENCY OF SURFACE WATER CONTAMINATION BY EDC

System size (population served)	NUMBER OF POSITIVE SYSTEMS							
	NORS	NOMS I	NOMS II	NOMS III	NSP	CWSS	RWS	Total
25-100	0	0	0	0	0	0	0	0
101-500	0	0	0	0	0	0	0	0
501-1,000	0	0	0	0	0	0	0	0
1,001-2,500	0	0	0	0	0	0	0	0
2,501-3,300	0	0	0	0	0	0	0	0
3,301-5,000	1	0	0	0	0	0	0	1
5,001-10,000	0	0	0	0	0	0	1	1
10,001-50,000	3	0	0	0	0	0	0	3
50,001-75,000	4	0	1	0	0	0	0	5
75,001-100,000	0	0	0	0	0	0	0	0
> 100,000	14	1	0	1	1	0	0	17
TOTALS	22*	1	1	1	1	0	1	27

*This value should be 6 since 16 samples were below the MQC.

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REFERENCES

Alumot, E., E. Nachtomi, E. Mandel, P. Holstein, A. Bondi and M. Herzbert. 1976. "Tolerance and Acceptable Daily Intake of Chlorinated Fumigants in the Rat Diet." Food Cosmet. Toxicol. 14(2):105-110.

Banerjee, S. and B.L. VanDuuren. 1978. Covalent binding of the carcinogen trichloroethylene to hepatic microsomal proteins and to exogenous DNA in vitro. Cancer Res. 38:776-780.

Banerjee, S. and B.L. VanDuuren. 1979. Binding of Carcinogenic Halogenated Hydrocarbons to Cell Macromolecules. J. Natl. Cancer Inst. 63:707-711.

Hooper, K., L.S. Gold and B.N. Ames, 1980. The Carcinogenic Potency of Ethylene Dichloride in Two Animal Bioassays: A Comparison of Inhalation and Gavage Studies. In: The Banbury Report No. 5: Ethylene Dichloride: A Potential Health Risk? Ames, B., Infante, P. and Reitz, R., Cold Spring Harbor, N.Y., Cold Spring Harbor Laboratory, pp. 65-78.

Hooper, K., L.S. Gold and B.N. Ames, 1980. The Carcinogenic Potency of Ethylene Dichloride in Two Animal Bioassays: A Comparison of Inhalation and Gavage Studies. Ibid. p 67

Jenssen, D., and C. Ramel, 1980. The micronucleus test as part of a short-term mutagenicity test program for the predicition of carcinogenicity evaluated by 143 agents tested. Mutat. Res., 75:191-202.

King, M.T., H. Beikirch, K. Eckhardt, E. Gocke and D. Wild. 1979. Mutagenicity Studies with X-ray Contrast Media, Analgesics, Antipyretics, Anthirheumatics and Some Other Pharmaceutical Drugs in Bacterial, Drosophila and Mammalian Test Systems. Mutat. Res. 66:33-43.

Lane, R.L., B.L. Riddle, and T.F. Borzelleca, 1982. Effects of 1,2-dichloroethane and 1,1,1-trichloroethane in drinking water on reproduction and development in meice. Toxicol. Appl. Pharmacol. 63:409-421.

Lutz, W.K., 1979. In vivo covalent binding of organic chemicals to DNA as a quantitative indicator in the process of chemical carcinogenesis. Mutat. Res., 65:289.

Maltoni, C., L. Valgimigli, and C. Scarnato, 1980. "Long-term Carcinogenic Bioassays on Ethylene Dichloride Administered by Inhalation to Rats and Mice." In: EDC: A Potential Health Risk? banbury Report 5/ Ames, B., Infante, P. and Reitz, R., eds. Cold Spring Harbor, NY. pp. 3-29.

National Academy of Sciences. 1977. Drinking Water and Health, Washington D.C. National Academy of Sciences. 1980. Drinking Water and Health, 3:111.

Nylander, P., H. Olofsson, B. Rasmuson and H. Svahlin, 1978. "Mutagenic Effects of Petrol in Drosophila Melanogaster: I. Effects of Benzene and 1,2-Dichloroethane. Mutat. Res. 17:163-167.

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Plotnick, Dr. H.G. (1980). Banbury Report 5: Ethylene Dichloride. A Potential Health Risk? p 50, Cold Spring Harbor symposium.

Rao, K.S., J.S. Murray, M.M. Deacon, J.A. John, L.L. Calhoun and J.T. Young, 1980. Teratogenicity and Reproductin Studies in Animals Inhaling Ethylene Dichloride. In: The Banbury Report No. 5. Ehtylene Dichloride: A Potential Health Risk? Ames, B., P. Infante and R. Reitz, eds. Cold Spring Harbor, N.Y. Cold Spring Harbor Laboratory. pp. 149-161.

Rao, K.S., J.S. Murray, M.M. Deacon, J.A. John, L.L. Calhoun and J.T. Young, 1980. Teratogenicity and Reproductin Studies in Animals Inhaling Ethylene Dichloride. Ibid. p 149-161.

Rapoport, I.A. 1960. The Reaction of Genic Proteins with 1,2-Dichloroethane. Dokl. Biol. Sci. 134:745.

Reitz, R.H., T.R. Fox, J.E. Ramsey, J.F. Quast, P.W. Langvandt, and P.G. Watanabe. 1982. Pharmacokinetics and macromolecular interactions of ethylene dichloride in rats after inhalation or gavage. Toxicol. Appl. Pharmacol., 62:190.

Shakarnis, V., 1969. Induction of X Chromosome Nondisjunctions and Recessive Sex Linked Lethal Mutations in Females of Drosophila Melanogaster by 1,2-Dichloroethane. Sov. Genet. 5(12):89-95.

Spencer, H.C., V.K. Rowe, E.M. Adams, D.D. McCollister and D.D. Irish, 1951. "Vapor Toxicity of Ethylene Dichloride Determined by Experiments on Laboratory Animals." Ind. Hyg. Occup. Med. 4:482-493.

Spreafica, F., E. Zuccato, M. Marcucci, M. Sirani, S. Paglialunga, M. Madonna, and E. Mussini. 1980. Pharmacokinetics of ethylene dichloride in rats treated by different routes and its long-term inhalation toxicity. Banbury Report 5: Ethylene Dichloride: A Health Risk? Cold Spring Harbor. p 107-129.

Theiss, J.C., G.D. Stoner, M.B. Shimkin and E.K. Weisburger, 1977. "Test for Carcinogenicity of Organic Contaminants of United STates Drinking Waters by Pulmonary Tumor Responses in Strain A Mice." Canc. Res. 37, 2717-2720.

Urosova, T.P., 1953. "The Possible Presence of Dichloroethane in Human Milk with Exposure in Industrial Conditions." Gigiena i. Sanitariy, 18:36-37.

Vozovaya, M.A., 1971. "Changes in the Estral Cycle of White Rats with Chronic Combined Exposure to Benzine and Dichloroethane Vapors." Akusherstovo i Ginekologiya (Kiev) 47:65-66.

Vozovaya, M.A., 1974. "Development of Progeny of Two Generations Obtained from Female Rats Subjected to the Action of Dichloroethane." Gig. Sanit. (7):25.

Vozovaya, M.A., 1975. "The Effect of Low Concentrations of Gasoline, Dichloroethane and Their Combination on the Reproductive Function of Animals and on the Development of Progeny." Gig. Tr. Prof Zabol. 7:20-23.

Vozovaya, N.A., 1976. "Effects of Low Concentrations of Gasoline, Dichloroethane and Their Combinatin on the Reproductive Function of Animals." Gig. Sanit. 6:100-102.

Vozovaya, M.A., 1977. "The Effect of Dichloroethane on the Sexual Cycle and Embryogenesis of Experimental Animals." Akusk. Ginekol. 2:57-59.

Vozovaya, M.A. and L.K. Malyarova, 1975. "Mechanism of Action of Ethylene Dichloride on the Fetus of Experimental Animals." Gig. Saint. 6:94-96.