BRIEFING REPORT

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External Review Draft

ENVIRONMENTAL ASPECTS OF VINYL/POLYVINYL CHLORIDE

NOTICE

This document is a preliminary draft. It has not been formally released by EPA and should not at this stage be construed to represent Agency policy. It is being circulated for comment on its technical accuracy and policy implications.

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PREFACE

This report was prepared by a Task Force convened under the direction of Dr. John F. Finklea, Director, National Environmental Research Center (NERC) in June, 1974. In a preliminary assessment of the environmental problems associated with vinyl chloride and polyvinyl chloride, an EPA Task Force under the direction of the Office of Toxic Substances determined that emissions of vinyl chloride monomer was primarily an air pollution problem. Accordingly, the Office of Air and Solid Waste was given the responsibility for an in-depth evaluation of the problem. This report was proposed as a part of this evaluation. The objective was to review and evaluate the current knowledge of vinyl chloride and polyvinyl chloride emissions into the environment as related to possible deleterous effects upon human health and welfare.

The units of parts per million (ppm), in lieu of metric units, have been used in this report to be consistent with other agencies currently involved in the national assessment of the vinyl chloride problem.

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1. SUMMARY AND CONCLUSIONS

1.1 SUMMARY

This report represents a review and evaluation of the available current scientific data relative to the health and welfare implications of environmental pollution resulting from the production and use of vinyl chloride and polyvinyl chloride. New information about this compound has become available and important new data may be forthcoming in the near future.

Vinyl chloride monomer (VCM) was first synthesized in 1837. The vinyl chloride monomer is a synthetic chemical derived from petrochemical feedstock and chlorine. Its principal use is in the production of a wide variety of useful plastic materials such as floor tile, phonograph records, pipes and electrical insulation, although it has also been used in other ways, for example, as an aerosol propellant. The production of vinyl chloride began in the United States in the 1930's, the first important use was in the manufacture of synthetic rubber. Production levels increased rapidly after World War II--the beginning of the industrial chemical era which has produced over 20,000 new chemical products. Vinyl chloride production in the U.S. was less than 45 million kilograms (kg) in 1943 but exceeded 2.9 billion kg in 1973. The annual growth rate in this industry is expected to exceed 10 percent per year through the 1980's. In the United States vinyl chloride monomer is produced at 15 plants and polyvinyl chloride (PVC) is produced at 37 plants.

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Approximately 1500 workers are engaged in the production of vinyl chloride, and approximately 5000 are engaged in the production of polyvinyl chloride. The demand for products and components manufactured from polyvinyl chloride is extensive due to its widespread use,

thus the impact of control actions will be felt beyond the VCM/PVC industry. Thousands of companies, large and small, and hundreds of thousands of workers are engaged in the manufacture of and/or use of plastic products made from PVC.

Only a very limited amount of VCM emission data from industrial sources is available. VCM loss estimates of approximately 6 percent have been reported, based primarily on materiel balance studies. Losses to the outdoor atmospheres from industrial sources may occur at a large number of points in the manufacturing processes and will vary depending upon the manufacturing facility.

Currently, emissions of vinyl chloride from VCM and PVC plants are estimated to exceed 90 million kg annually. It is estimated that 90 percent of all vinyl chloride atmospheric emissions are believed to emanate from polyvinyl chloride plants. Monomer plants emit less than 10 percent of the total. Emissions of VCM from fabricating plants and from fabricated products may also occur, but at present there are no data to quantify what those emissions may be. The concentration of residual monomer in PVC powder that is fabricated into final products is an important determinant of VCM emissions in both these cases. ugitive emissions contribute a significant fraction to total VCM emissions, particularly in PVC plants, and these emissions are an important limiting factor in determining the degree of emissions control that can be achieved.

Technology may currently be available to reduce vinyl chloride emissions from VCM plants by as much as 90 percent and from PVC plants by as much as 75 percent. Control of emissions from PVC plants is a more difficult problem which may require complex process changes. Means of controlling emissions from PVC plants and from fabrication processes are yet to be determined.

Polyvinyl chloride plastics usually are not readily biodegradable. Incineration (without scrubbing) of polyvinyl chloride plastics results in the emission of hydrogen chloride gas, but not VCM. Experimental studies indicate that vegetational injury symptoms for ethylene and vinyl chloride are identical; however, no known information showing vegetational damage around VCM manufacturing or processing plants exists.

Vinyl chloride is a chlorinated olefinic hydrocarbon monomer which is a gas at ambient temperatures and atmospheric pressure. It is normally shipped and stored as a liquid under pressure. It is flammable, explosive, and only slightly soluble in water. VCM is about two times heavier than air. Analysis of vinyl chloride usually reveals trace amounts of organic impurities, such as acetylene, 1,3-butadiene, methyl chloride, vinylidine, and vinyl acetate. Polyvinyl chloride contains residual entrapped VCM in the parts per million range. The entrapped concentration is dependent upon the production process and can range from 0.1 to several (5-8) thousand ppm, which can be liberated during fabrication, particularly when heated. The production of VCM/PVC involves the use of a wide variety of chemicals other than VCM which also may contribute to adverse health effects under occupational circumstances.

There are few data on exposure levels of vinyl chloride in ambient air. The work place peak exposures in the past may at times have exceeded thousands of ppm; however, the average concentration would have been less. Limited atmospheric vinyl chloride concentration measurements have been made in the vicinity [0 to 8 kilometers (km)] of VCM/PVC production sources. In over 90 percent of the cases the peak concentrations have been below 1 ppm;however, one peak value (grab sample) of 33 ppm has been observed. A few twenty-four-hour average values of 1 to 3 ppm, at distances of 0.8 to 8 km from the source, have also been measured, probably in the downwind plume, although over 90 percent of 24-hour measurements were below 1 ppm.

Because of the sampling and analytical procedures used, the accuracy of these measurements may be no better than ± 100%.

Available atmospheric VCM data have been obtained using a variety of sampling and analytical techniques with varying degrees of sensitivity and accuracy. Consequently, the data are not directly comparable. Standard sampling and analytical procedures have not been established and practiced. Continuous monitoring methods suitable for field use are not available. Measurement methodology is adequate, but has not yet been applied to the problem of atmospheric and source sampling for VCM. The nature of VCM/PVC manufacturing facilities,particularly the older plants, is such that conventional source monitoring techniques may not be applicable due to the discontinuous nature of emissions. Using an atmospheric

dispersion model, estimates of VCM concentration in a downwind plume indicate that hourly integrated concentrations of 1 to 30 ppm might be expected depending upon atmospheric wind and stability conditions. The measured values and the values predicted by the model are the same order of magnitude.

Only limited laboratory studies have been made regarding photochemical reactions of VCM. Vinyl chloride does undergo atmospheric reactions in the presence of nitrogen oxides and solar radiation; although the reaction rate is slower than with other hydrocarbons known to be in the atmosphere. Reactions products of VCM photooxidation include CO, formaldehyde, formic acid, formyl chloride and hydrogen chloride. In addition, VC may indirectly contribute to the buildup of ozone. The extent to which VCM contributes to these other components in photochemical smog is not known. The estimated half-life of VCM in the atmosphere is about 6 hours.

The principle route of human exposure to vinyl chloride is thought to be through air inhalation, although exposure could occur from ingestion of food and water, and from skin contact. There is no evidence to indicate that vinyl chloride exists in normal drinking water, or in foods, except possibly in special cases involving leaching of VCM from wrapping and storage materials. Use of vinyl chloride as a propellant in aerosol products has also recently been discontinued so that this source of exposure, though significant in past years, is not anticipated to represent a problem in the future.

Acute animal toxicity to VCM was first reported in 1938. Toxic manifestations in experimental animals and man included eye irritation, increased motor activity leading to tremor and loss of muscular

coordination, and finally narcosis, and cardiac irregularities. Exposure concentrations in these acute studies ranged up to 400,000 ppm for periods extending from 30 minutes to daily exposure of several hours.

Short-term acute human experiments (intermittent 5 minute exposures separated by 6 hours over a period of 3 days) with concentrations ranging up to 20,000 ppm produced acute toxic effects at levels above 8,000 ppm.

Chronic toxicity effects due to VCM in experimental animals include cancer, damage to the liver, spleen, kidney, lungs, brain and nerve bundles. Some of the pathological lesions observed in these animal experiments were similar to those later observed in humans engaged in the production and handling of vinyl chloride.

Our present knowledge of undesirable health effects associated with vinyl chloride exposure in man comes primarily from recent occupational observations, complemented by additional animal data. Between 1949 and 1966 an increased incidence of excessive liver damage and acroosteolysis, a degenerative disease affecting bones and fingertips were reported among vinyl chloride workers in Europe. Studies in Germany revealed evidence of liver pathology in an abnormally high percentage of PVC production workers with a history of employment ranging from 1.5 to 21 years, but exposure levels responsible for this damage are not known. Since early occupational health studies often reported acute toxic effects, similar to those found in the human experiments previously mentioned (dizziness, headaches, nausea, etc.), it can be assumed that peak exposure levels of several thousand ppm were experienced at times.

Available air monitoring data in PVC plants during the period 1950-1959 indicates that the highest time weighted average exposures in these facilities were in the range 120-385 ppm. Studies in Europe

and the United States since 1966 tend to confirm the earlier findings in Europe. These studies include observations of liver damage among workers not directly involved in the actual production of PVC. The frequency and severity of liver pathology among PVC workers has been related to the length of exposure; i.e. being most common in workers with an exposure history in excess of 10 years. In one study, the degree of damage did not appear to decrease with increasing intervals of time between the last exposure and taking of biopsies.

To date 15 cases of liver angiosarcoma have been reported among workers with a history of exposure to vinyl chloride in the United States and 10 such cases have been reported from Europe. Most, but not all, of these reported cases have been among workers involved directly in PVC production. Cases of liver angiosarcoma have been reported in 1 U.S. and 3 European workers exposed to VCM, but not directly involved in PVC production. These cases suggest that exposure to vinyl chloride at lower levels than usually encountered in PVC production plants may be capable of causing liver angiosarcoma. Two community cases of liver angiosarcoma have also been reported in persons whose residences were in the vicinity of industrial VCM emission sources, which raises the question as to whether or not ambient air levels of VCM may, under certain circumstances, contribute to this disease. Additional studies are, however, necessary to confirm this possibility. Based upon the present reporting methods, angiosarcoma is a rare form of liver cancer in the general population, and for all practical purposes, is invariably fatal. The latent period for liver

angiosarcoma has been estimated at about 20 years, based upon medical records on occupational exposure cases. The levels and durations of exposure necessary to induce liver angiosarcoma in the occupational or the general population living in the vicinity of emissions sources are not precisely known.

Compared to the general population, the relative risk of liver angiosarcoma among workers exposed in the past to high levels of vinyl chloride is estimated at approximately 3,000. Such a relative risk represents a striking statistically significant difference ($p << 0.01$) in the frequency of liver angiosarcoma among those exposed to high levels of vinyl chloride compared to those in the general population not exposed to VC, or exposed to much lower levels.

While the focus of attention has been on liver angiosarcoma, it should be noted that a number of industrial studies indicate that the risk of developing other cancers besides liver angiosarcoma, particularly lung and brain cancer, is also related to exposure to vinyl chloride. The multiple cancer risk associated with vinyl chloride also is supported by the available animal studies.

Chronic toxic effects of VCM have been studied in a variety of animal species. Angiosarcoma of the liver has been observed in rats, hamsters, and mice exposed to vinyl chloride. Angiosarcoma was not observed in all animal studies. In two of these, rats and mice, liver angiosarcoma has been produced by exposures as low as 50 ppm. The frequency of liver angiosarcoma in experimental animals appears to be dose-dependent above 50 ppm, but the shape of the dose-response curve below 50 ppm is not known. Duration of exposure has been shown to affect the tumor response in animals. Other damage,

including tumors of the lung, spleen, and kidneys has been observed in animals exposed to vinyl chloride.

VCM/PVC workers are exposed to a variety of chemicals which may be carcinogens and/or liver toxins in addition to VCM. Such a complex exposure pattern makes it difficult to draw final conclusions regarding the specific role played by vinyl chloride in the development of liver cancer. However, the results of animal experiments demonstrating liver angiosarcoma from exposure to VCM in 3 species, coupled with occupational data implies that vinyl chloride is a causal factor in the development of liver angiosarcoma.

Although actual VCM exposure levels responsible for liver angiosarcoma and/or other cancers in man are not precisely known, limited measurements around VCM/PVC production facilities indicate that contiguous populations are being exposed to low levels of vinyl chloride, which may impose a health risk. The presence or importance of chemical co-factors besides vinyl chloride in the etiology of liver angiosarcoma is not well defined, though other chemicals besides VCM; i.e., thorotrast and arsenicals have been associated with liver angiosarcoma in man. Health implications relating to PVC dust particles containing residual VCM have not been well studied.

Data in animals and man for the lower end, less than 50 ppm, of the VCM dose response curve are not available. Attempts to extrapolate animal dose response curves to define a presumed "no-effect" level are fraught

with problems which impact upon the state-of-the art in cancer research, and the availability of resources required to conduct long time chronic studies. Similarly it is difficult to extrapolate data in experimental animals directly to man who may be more or less sensitive than animals to given chem... structures. These problems reflect important gaps in our knowledge concerning environmentally related cancers.

The mechanism for producing liver angiosarcoma by the inhalation of VC has been postulated but has not been confirmed. It is also not known whether the mechanism can be activated by intermittent peak exposures or whether frequent, or essentially continuous, exposure to low concentrations is sufficient to cause cancers to develop.

1.2 CONCLUSIONS

Precise data that indicate the degree to which the general population is exposed to vinyl chloride, and its consequent effects, are not available. However, available data supports the following tentative conclusions:

1. Vinyl chloride in the atmosphere in the vicinity of emission sources is a potential health hazard.

2. Occupational cases of angiosarcoma have been observed among PVC production workers predominantly with long-term exposure (greater than 20 years) to VCM at unknown, but suspected high, concentrations. However, cases of liver angiosarcoma have been reported among workers exposed to VCM but not directly involved in PVC production, raising the question of effects at lower levels of exposure. ?

3. Observations among workers and in experimental animals indicate that there is a multiple cancer risk from exposure to vinyl chloride.

and liver angiosarcoma and other

4. The mechanism and dose-response relationships between vinyl chloride/ at community exposure levels are not known.

5. Persons living in the immediate vicinity of VCM/PVC plants have been exposed an unknown number of times to 24-hour average concentrations of VCM of at least 1 ppm with occasional peak exposures of 30 ppm, however, over 90% of the observations have been less than 1 ppm.

6. Available monitoring data indicate that exposure to VCM around VCM/PVC plants is a local problem confined to within about an 8 km radius. Data in the vicinity of PVC product fabricating plants and other sources are not available.

7. Interim methodology is available for monitoring VCM in the atmosphere, but a standard monitoring system has not been developed.

8. Air inhalation is the primary route of human exposure to VCM.

9. VCM is a primary pollutant, but is atmospherically active and hence a precusor for other pollutants. Little is known about transformation, transport and removal processes. The half-life in sunlight is about 6 hours.

10. VCM in drinking water or food presently does not appear to be a problem.

11. There are no known natural sources of VCM.

12. The emissions data identifying specific point sources in PVC and VCM plants is based on calculationsand estimates and is not sufficiently accurate to serve as the basis for the formulation of a quantitative emissions control strategy.

13. The practicality and effectiveness of carbon sorption systems, surveillence-maintenance programs, and deep stripping of the polymer

remain to be demonstrated as commercially visible control techniques.

14. There are no known studies of damage to vegetation in areas surrounding VCM/PVC plants.

2. INTRODUCTION

Historically, national and international commerce has established markets for new products rarely with due consideration being given to the environmental consequences of the manufacture, use, and disposal of the new products. Consequently, air, water, soil and biota have been contaminated with a wide variety of natural and snythetic chemical compounds that may threaten public health and welfare. The contributory role of a number of chemicals in the production of cancer and other chronic degenerative disease is well known. In the absence of appropriate pre-market testing, assessment of environmental health hazards for many chemical compounds often depends upon retrospective analyses after these products have attained broad multi-media distribution. Establishing prudent standards of environmental quality depends upon the availability of a broad integrated data base that is sufficiently quantitative to permit appropriate risk and benefit assessments to be made.

Until recently, the principal environmental concerns associated with the plastic industry has been waste-water effluents from industrial facilities and the solid waste problems associated with accumulation and disposal of various plastic materials.

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In 1971 the release of phthalate plasticizers from flexible plastic material not only aroused public health concern but served to elicidate a mechanism of transporting potentially hazardous material in a wide-spread fashion. More recent attention has focused upon serious occupational health hazards associated with exposure to vinyl chloride. The basis for this concern is evidence of vinyl chloride carcinogenicity in experimental animals and man.

The predominate commercial importance of vinyl chloride lies in the manufacture of polyvinyl chloride resins which are subsequently manufactured into a large number of useful plastic products. Vinyl chloride may be disseminated on a broad scale as an unreacted monomer entrapped in finished products such as polyvinyl polymers and co-polymers similar to that of the phthalate plasticizers. During the past thirty years, vinyl chloride production has increased from less than 45 million kg in 1943 to more than 2.4 billion kg in 1973. Estimated loss from industrial facilities (both monomer and polymer production) have been placed at over 90 million kg in 1973.

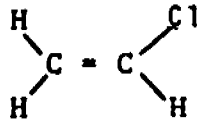
The primary purpose of this report is to provide an interpretive and where possible, quantitative summary of available biomedical effects of vinyl chloride. In this regard, attention is given to gaps in the existing data base.

Emphasis has been placed upon recent health effects developments, efforts have been made to review and place into perspective the older literature as well.

3. CHEMICAL AND PHYSICAL PROPERTIES

3.1 Physical Properties

Vinyl chloride (VC) is a chloroolefinic hydrocarbon with a density of twice that of air having the structural formula shown below and a molecular weight of 62.5.



Since VC boils at -13.37°C, it is a gas at normal atmospheric temperature and pressure. It melts at -160°C, and therefore is a solid only at very low temperatures. Vinyl chloride is highly flammable having a flash point of -108°F. The explosive limits are from 4 to 22 percent VC in air by volume. The presence of a chlorine atom in the ethylene molecule changes the dipole moment from 0 to 1.45 debye units. The corresponding saturated hydrocarbon, cloroethane (ethylene chloride) has a dipole moment of 2.05. Since vinyl chloride can be manufactured starting with ethylene or ethylene dichloride, some of the physical properties are changed from the parent compounds by the presence of chlorine and the double bond. These properties and the phenomenon of resonance reduce the reactivity of VCM. VCM is soluble in organic solvents, but sparingly soluble in pure water. The quantity of the VCM that dissolves in water will depend on the partial pressure of the gas above the solution. VCM reacts minimally with pure

water. If the partial pressure of the gas above the water is reduced VCM will escape into the gas phase. Therefore, water that contains VCM would release the gas to the ambient air or chemical reactions occur with water impurities which might tend to inhibit escape of vinyl chloride. Certain salts do have the ability to combine with VCM; soluble silver and copper salts increase the solubility of VCM in H_2O by forming complexes, for example. Besides the previously mentioned salts, olefins will also complex with $FeCl_2$, Pt Cl_2, $IrCl_2$, Hg_2Cl_2 and a host of other salts. Hence, the residence time availability of VCM in water could be affected by the presence of certain salts. The principal physical characteristics of vinyl chloride are given in Table 3.1.

3.2 CHEMICAL PROPERTIES[2-6]

The halogen atom attached to the carbon to carbon double bond is generally inert. When forced to react, HCl is extracted from VC with the resulting formation of acetylene. Similarly, the hydrogen atom attached to double bonded carbon atoms are highly stable in substitution reactions. The order of reactivity of hydrogen atom is allylic $>3^{\circ} >2^{\circ} >1^{\circ} >CH_4 >$ vinylic.

The importance of vinyl chloride lies in its ability to polymerize readily in the presence of ultraviolet light or peroxides. The product is a highly useful plastic containing the basic structure $(CH_2 - CC: H)_n$.

The most important reactions of the olefinic hydrocarbons are related to additions of various compounds to the double bond, e.g., hydrogen peroxide, halogens, haloacids, halohydrins, oxides of nitrogen, sulfuric acid and ozone. Only a few, namely, hydrogen peroxide, oxides of nitrogen, sulfuric acid, and of course ozone, should be of some importance in ambient air. The ease of formation of free radicals of importance in photochemical activity is allyl >3° >2° >1° > CH_3 > vinyl. However, the stability of the free radical is in the reverse order.

Table 3.1. PHYSICAL CHARACTERISTICS OF VINYL CHLORIDE[b]

Formula	$CH_2 \cdot CHCl$
Molecular weight	62.50
Vapor pressure 21.1°C	34 ps ig (2.4 kg/cm^2 gauge)
Specific volume 21.1°C	6.2 cu ft/lb (387.0 ml/g)
Boiling point 1 atm	7.0°F (-13.9°C)
Freezing point 1 atm	-255.5°F (-159.7°C)
Specific gravity, gas 15°C., 1 atm (air = 1)	2.15
Density, liquid - 20°C	0.9834
Critical temperature	317.1°F (158.4°C)
Critical pressure	774.7 ps ia (52.7 atm.) (54.4 kg/cm^2 absolute)
Critical density	0.370 g/ml
Latent heat of vaporization b.p	79.84 cal/g
Latent heat of fusion m.p	18.14 cal/g
Specific heat	
Liquid 20°C	0.38 cal/(g) (°C)
Gas 25°C., 1 atm., Cp	0.205 cal/(g)(°C)
Viscosity, liquid -20°C	0.278 centistoke (0.2734 centipoise)
Flammable limits in air	4.0-22.0 percent (by volume)
Autoignition temperature	881.6°F (472°C)
Dielectric constant 17.2°C	6.26
Surface tension -20°C	22.27 dynes/cm
Refractive index, n_D^{-10}	1.4046
Solubility in water 25°C, 1 atm	0.11 g 100 g water

VCM is soluble in alcohol, very soluble in ether and carbon tetrachloride.

Synonyms: cloroethene, chloroethylene

Conversion factors at 25°C and 760 mm Hg.
1 ppm = 2,56 mg/m^3
1 mg/liter = 391 ppm

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Table 4.1

POSSIBLE INTERFERENCES WITH VINYL CHLORIDE ANALYSIS [1]

Compound	Vinyl Chloride Analytical Bands (cm^{-1})			
	1626	1020	917	730
Acrylonitrile			W	
Allyl Chloride			S	W
Chlorobromomethane				W
Chloroform				W
Ethylene		M	S	
Ethylene Dichloride				S
Freon-11			W	
Freon-12	W		S	
Freon-113		S	M	W
Methacrylonitrile	W	W	S	W
Methyl Chloroform				S
Methyl Chloride		W		M
Methyl Methacrylate	W		W	
Perchloroethylene			S	
Styrene			M	
Tetrahydrofuran			M	
Trichloroethylene			M	
Toluene	W		W	S
Vinyl Acetate	M	S	W	W
Vinylidine Chloride	S			
Vinylidine Fluoride	S		S	

KEY: W = WEAK M = MODERATE S = STRONG

4. MEASUREMENT TECHNIQUES

4.1. ENVIRONMENTAL AIR

In selecting methods suitable for measuring VCM in ambient air, two factors must be considered. The method employed must be capable of measuring in the part per million to the part per billion range, and, because emissions are discontinuous, the method must be capable of responding to high concentration peaks as well as low level backgrounds.

4.1.1 Spectrophotometry

To design or describe a useful measurement technique or analytical method for a particular purpose requires that three major criteria be satisfied: sensitivity, accuracy and specifity. In addition practicality and economics are important considerations in the development of new analytical methods. As a general rule, it is most desirable to measure a pollutant or chemical specie directly in the matrix or phase--gas, liquid or solid--in which the material is generally encountered. This rule precludes any loss or transformation of the analyte to a non-detectable form. Whenever possible, in the following descriptions of analytical techniques, the above criteria will be addressed.

VCM absorbs infra red (IR) radiation in the gas phase. The absorption bands at 941 or 917 cm^{-1} have been commonly used to quantify VC. However, the method is not entirely specific for VCM as interfering substances (Table 4.1) are encountered in ambient air.[1] Multiband measurement and data processing techniques are available to correct for these interferences, but additional instrumentation is required. The Fourier transformation system is an excellent example of a refinement in this technique. The cost, however, of this type of system would be prohibitive for routine

monitoring. Infrared analyzers are not sufficiently sensitive for trace quantities of VCM in air since effective optical paths of 20 meters are required to achieve a lower limit of detection of 1 ppm. Accuracies of ± 10 percent are attainable when properly calibrated with standard gas mixture. Although the technique is adaptable to continuous monitoring, it is impractical as a multipoint detector of the type generally required to characterize a problem area. Economics dictate this technique for use as a research tool or as a laboratory instrument. Air samples, either instantaneous or integrated, can be collected, concentrated if necessary, and returned to a central laboratory for analyses by IR.

4.1.2 Gas Chromatography

Gas chromatography (GC) is an analytical technique that separates a complex mixture into its component parts by partitioning the chemical material between a gas and a liquid or solid. The technique is highly popular because of its versatility in solving analytical problems. A wide variety of materials and conditions are available that can be used to achieve separations effectively and inexpensively, even for closely related compounds.

A list of column materials that have been used to separate vinyl chloride and related compounds is shown in Table 4.2. This by no means is a complete list and there are other systems that can be designed.

It is difficult to select the best column material from the available literature, because quantitative data on column efficiencies and height equivalent to a theoretical plate are not generally

Table 4.2 COLUMN MATERIALS AND LIQUID SUBSTRATES SEPARATING VINYL CHLORIDE

Column materials and liquid substrates	References
Porapak, Q	Forris (1960) .12
Silicone oil DC 550	Levadie (1960) .18
Silver nitrate/ethylene glycol	Smith B. (1962) .17
30% silicone oil and polyethylene glycol	Vyakhirev (1962) .2
Disodecyl phthalate/carbowax	Hannon (1963) .19
Carbowax 4000	Newman (1963) .16
25% $O\text{-}C_6H_4$ $(CO_2Bu)_2$	Martur (1966) .5
15 to 15% silicon rubber SE-30	Hinshaw (1966) .6
Silicone grease	Esposito (1967) .7
Porapak, -S	Koenig (1967) .10
Poly (methyl phenyl siloxane)	Popova (1967) .10
Tricresyl phosphate	Vlasov (1970) .14
30% dioctyl sebacate	Zalinyan (1972) .15
Carbowax 1500 or carbopack A	Brown D. Region IV.23 Interim procedure

provided, nor are the objectives of the reported method always similar to ours. Therefore, laboratory evaluation is required to ascertain the best column material that effectively separates VCM from all possible interferences that may be encountered in ambient air. It is particularly important that VCM is separated from hydrocarbons and Freons(R). Alternatively, more specific detectors must be used in combination with GC.

Detectors that are used in combination with GC columns are also varied. Highly selective and highly sensitive detectors are available which will detect quantities of material down to 10^{-12} grams. Completely automated GC are commercially available for environmental monitoring. On some of these instruments all that needs to be changed are the column materials and operational parameters. However, with rare exceptions, measurements are not made continuously but are made by taking instantaneous samples at short periodic intervals.

4.1.2.1 Detectors--The flame ionization detector (FID) is a general purpose detector which responds to most organic compounds, has a wide linear range of several orders of magnitude, and sensitivity down to parts per billion. The response to a chemical compound generally varies with the number of carbon atoms. However, certain carbon atoms have reduced or no response when the carbon atom is attached to atoms other than hydrogen; e.g., Cl, O,S. The detector is insensitive to almost all organic gases and compounds. The minimum detectable concentration for VCM using a 10 ml sample of gas is 0.01 ppm. When coupled to a GC column to achieve separation, the FID has been the detector of choice because of its sensitivity and minimal cost for the analysis of complex

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organic mixtures. The combination of GC-FID has been used under field conditions, but power requirements and the need for hydrogen gas reduce the practicality of the instruments for routine monitoring.

The thermal conductivity detection (TC) is mentioned only for historical purposes. The detector measures changes in heat capacity of the carrier gas, usually helium or hydrogen, when materials elute from the column. The sensitivity is low when compared to other available detectors. It is not suitable for trace analysis. In addition, TC responds to water vapor; this causes problems in identifying and measuring compounds of interest.

A third group of detectors fall under the general classification of D.C. ion chambers. These include argon ionization, helium ionization, micro-cross section detectors and, most important of all, electron capture detectors. The argon detector consists of 2 or 3 parallel, electrodes and a radioactive source, usually Sr^{90}, which excites the argon carrier gas. When chemical compounds elute from the column they are ionized by the excited argon. Under a voltage gradient up to 1,000 V these ions produce an increase in current flow across the plates or electrodes which is proportional to the concentration of the eluting material. The sensitivity is ~~food,~~ 6000 but it is non-specific and temperamental.

The design of the helium detector is similar to the argon detector, except that helium is used as the carrier gas. Voltage gradients as high as 2,000 V can be applied across the plates. Radioactive hydrogen, tritium, is frequently used as the excitation source. This detector is also temperamental, highly sensitive and non-specific, but is usually recommended for traces of inorganic gases to be detected with gas-solid

chromatography.

The electron capture (EC) detector is of similar design as the other DC-ion chambers. Nitrogen or argon is used as the carrier gas and tritium or Ni^{63} as the radioactive sources. Low voltages 5 to 25 volts are applied across the plates usually in a pulsating mode to eliminate polarization of the electrodes. The detector is specific and highly sensitive to halogenated materials and other materials that absorb electrons. It has a smaller dynamic range and is more temperamental than the FID. Sensitivities for VCM have been reported to be less than that with the FID because of the presence of a single chlorine atom in the molecule.[4,24] More recent data indicates sensitivities tabulated[24] in Table 4.3.

Table 4.3 SENSITIVITY OF SELECTED DETECTOR USED IN GAS CHROMOTOGRAPHY

	TC	Argon D	FID	EC
Vinyl chloride	2×10^{-6} g	1.9×10^{-9} g	2.2×10^{-9} g	2.3×10^{-9} g
Trichloroethylene	2.2×10^{-6} g	1.0×10^{-8} g	8.5×10^{-9} g	2.0×10^{-11} g

The GC-EC has the advantage of requiring only one gas cylinder of nitrogen, and, because of its specificity, complete resolution of VCM by the GC column is no longer mandatory. Battery operated GC-EC instruments have been manufactured commercially.

The micro coulometer is a highly sensitive and electrochemical detector of the chloride ion. The specificity of this detector is increased when used with gas chromatography. Chlorinated hydrocarbons, such as VCM are pyrolyzed as they elute from the column to form gaseous HCI which reacts

regenerates Ag^+ until the electrical balance is restored. The detector will also respond to any substance which precipitates Ag. However, depending on column and pyrolysis conditions, these potential interferences can be eliminated. With electrochemical efficiency of close to 100 percent, the coulombs generated to restore the balance is proportional to the quantity of Cl^- in accordance with Faraday's law. The detector is highly accurate because the coulomb is a primary standard, and hence standard reference materials are not absolutely essential. The sensitivity of the detector for VCM is of the order of a few nanograms. Power requirements make this system impractical for field instrument use, but it is excellent in the laboratory technique.

Another electrochemical detector is the conductivity device developed by Coulson for use with gas chromatography.[28,29] The conductivity detector measures water soluble ions or gases that produce soluble ions when they react with water. The effluent material is either oxidized or reduced in a small furnace prior to reaching the detector. Depending on the mode of operation, the detector response can be restricted to HCl, SO_2 or SO_3. High sensitivity is attainable because of the solubility of these gases in water and the high mobility of the hydrogen ion produced. Sensitivity of the order of a few nanograms is possible. The ultimate sensitivity depends on the geometry or the cell constant. More recently the conductivity cell has been designed by Hall to yield higher sensitivities than the Coulson detector.[30] Again, specific detectors reduce the demand on the column to resolve compounds with elution times close to VCM. Power requirements reduce the practicality of this detector under field

conditions.

The Beilstein test is a classical flame test for detecting halogens in the presence of copper. This test is the principle for a flame photometric detector that has been used as a gas chromatographic detector. It measures the characteristic spectrum produced by halogenated substances with a photomultipler tube. The sensitivity of this detector has been enhanced by use of iridium metal.[31] It may be useful as a continuous monitor for gaseous halogenated substances without gas chromatography. By use of a filter to remove inorganic halogens, this measuring technique would give an index of the total quantity of halogenated materials in a given area. However, to achieve specificity for VCM a GC column would be required. Practicality for field use is equivalent to other flame detectors.

Chemiluminescence detectors are used in continuous monitors that measure the quantity and type of light that is produced by reacting certain compounds with ozone - the determination of ozone by reacting with ethylene or the determination of NO by reacting with ozone Recently the monitor has been adopted by EPA scientists to measure VCM. However, to obtain specificity, a gas chromatographic column is required. Current evaluation of the monitor indicates a sensitivity of a few parts per billion is achievable.

The alkali flame ionization detector and stacked thermionic detectors have also been used as GC detectors to measure halogenated compounds. The mass spectrometry when connected to GC column is particularly useful in identifying an unknown compound and for unequivocal confirmation of VCM. All of these detectors have sensitivities within one or two orders of magnitude

of each other. The necessity of one or more gas cylinders and power requirements limit their utility in the field instrument.

Some techniques are more selective than others, some are too expensive for field application and some require more extensive evaluation for the purpose of measuring VCM.

4.1.3 Other Methods of Analysis

Coulometry has been used to measure olefinic hydrocarbon by reaction with electrogenerated Br_2. This technique is not useful for measuring VCM in ambient air because of the long reaction time required for the bromination of olefins. In addition, reducing substances such as SO_2 would interfere by consuming bromine. Oxidant would cause a negative interference. Wet chemical methods[22,23] have also been developed based on the bromination of VCM, then titrating excess bromine. The sensitivity is only 0.1 mg. Olefins, aromatic compounds that readily add bromine and and reducing agents interfere with this wet chemical method.

Vinyl chloride in air has been analyzed colorimetrically by collection on activated carbon.[29] The VCM was extracted and oxidized to formaldehyde. The formaldehyde was determined in the usual manner by reacting with chromotropic acid, however, ethylene and methanol interfere. Sensitivity is only a few micrograms.

Polarography[20,21] has been used to measure VCM by bromination at the dropping mercury electrode. When this procedure was applied to volatile VCM from plastics, it gave higher result than the analysis of total chloride. Hence interfering volatile materials are present. Sensitivity for VCM was only 70 µg/ml.

4.1.4 Sampling and Laboratory Analyses

The most inexpensive approach to monitoring VCM would be to collect samples in a suitable manner and return them to a central laboratory for analysis. Using this approach, samples could be collected throughout a suspected problem area with a minimum of power, a minimum of equipment, and with unskilled personnel. Grab samples are collected, as described in the interim procedure [23] in Tedlar bags or stainless steel canisters. Varying degrees of instability from 0 to 10 percent per day have been reported when VCM in air was stored in Tedlar bags. It is possible leaky bags are responsible for losses. However, VCM in pure air appears to be stable. In polluted air, particularly in the presence of ozone, reactions are expected to continue. Direct photoexcitation of VCM are not expected to occur because solar radiation below 290 nm does not reach the lower atmosphere. Hence, this solar energy is not absorbed by VCM in ambient air. However, in the presence of nitrogen dioxide which absorbs solar radiation about 2900 nm, secondary reactions involving ozone (produced by the photolysis of NO_2) and VCM occur. It may be possible to spike the air sample with a free radical or ozone scavenger to stabilize the VCM in the sample. Tedlar bags used for sampling create a storage and handling problem. Wall losses and permeability of the VCM through the walls of the plastic bag do not appear to be a problem with Tedlar at concentrations in the range of 10 ppm.

Evacuated stainless steel canisters have the advantages of being more rugged, and more easily stored and transported than Tedlar bags. These canisters need only a silicone septum through which a needle can be inserted to evacuate the system to a low pressure. The needle is withdrawn and the septum seals itself maintaining a vacuum until a sample is ready to be taken. At the sampling site, a needle is again inserted and polluted air allowed to fill the canister. The needle is withdrawn and the septum seals itself again. At the laboratory, an aliquot of the sample is removed with a gas tight syringe and injected directly into a gas chromatograph or other measuring device.

The above procedure yields a short term concentration and does not yield a total dosage It appears necessary - particularly because of the discontinuous nature of the emissions that produce pockets of high concentration of VCM-- that some accurate measure of the total or average dosage over a prescribed period be obtained.

4.1.5 Liquid Scrubbers

Very little information is available concerning the use of liquid scrubbers for the collection of VCM. The physical properties of VCM are such that it is not easily trapped by liquid unless some complexation reactions can be produced. Certain salts have been reported to complex VCM, but these salts have not been thoroughly investigated for this purpose. In addition, liquid scrubbers for monitoring air pollutants, introduce collection, handling and stability problems that render the technique impractical.

4.1.6 Solid Scrubbers

Solid scrubbers are more easily handled, transported and have fewer collection problems. Activated charcoal has been extremely useful for the collection of gases and vapors including VCM. The capacity of charcoal for VCM is limited. Hence, problems have been reported resulting from the use of small tubes and large sampling volumes. It is imperative that all newly purchased charcoal be reactivated under nitrogen to maintain its absorption capacity and to remove impurties that may interfere in the analyses. Charcoal was selected as the collection medium in the interim procedure in order to to obtain time weighted averages. The use of multiple sections was specified to ascertain the quantity of charcoal required under field conditions. It is not yet known how the procedure will respond under field conditions and relative humidities close to 100 percent to determine the quantity of charcoal required to collect VCM under the most adverse conditions. Other solid scrubbers may be more suitable for collection of VCM.

Hollis[3] reported long retention times of low molecular weight hydrocarbons and halogenated hydrocarbons on porous polyaromatic polymer beads. Williams and Umstead[32] determined a number of halogenated hydrocarbons by concentrating the sample on Parapak Q & S.

The materials were thermally desorbed at 100 °C for analysis. They used the micro coulometer with the silver cell to determine VCM at the 10 parts per billion level. Lonneman[25] used carbowax under crogenic conditions to concentrate the sample and analyze concentrations of 100 parts per trillion by gas chromatography. More recently, Bellar[26] successfully concentrated VCM from aqueous solution by adsorbing on carbonsieve B. Quantitative recoveries were obtained from aqueous solution containing from 5 ng to 5 µg of VCM. All solid scrubbers should be evaluated under simulated field conditions. Permeation devices[33] are available commerically which will generate low levels of VCM in air and the resulting mixture diluted with humid air. In this manner, collection and recovery efficiencies can be more definitively established. The stability of VCM on storage in the presence of reactive pollutants in the atmosphere is not known. Some investigators have reported that VC might be polymerizing on these scrubbers. It has been demonstrated by Lajos and Paduly[27] that hydroquinone improved recoveries of VCM from charcoal without reducing its adsorption capacity.

4.1.7 Sample Preparation

Grab samples present no problems since aliquots are injected directly into a gas chromatograph, if the range of interest is greater than 0.02 ppm. Air samples can be concentrated as previously described, to detect levels of 0.2 ppb, if a sufficient sample is available. Good recoveries from charcoal have been reported by Brown[23] by extracting with CS_2. This is an

excellant solvent for gas chromatography when using the FID This detector gives no response to CS under the usual operating condition and solvent interferences are eliminated. Keenman,[1] however, observed that appreciable quantities of VCM evaporated into the head space above the liquid when CS_2 was used as the extractant for VCM. Total recovery of VCM in both the liquid and the gas phase was only 80%. When VCM was extracted with tetrahydrofuran (THF), he obtained a recovery of 88 percent with less diffusing into the head space than was evident with CS_2,

4.1.8 Automated Monitoring

Completely automated monitoring instruments, which are commercially available, can be easily modified to measure vinyl chloride. For example, the carbon monoxide - methane analyzer, which uses a precolumn, a gas chromatographic column, and flame ionization detector may be used as a vinyl chloride instrument by simply changing the column packing material and operational parameters. The precolumn removes most of the higher molecular hydrocarbons and maintains the integrity of the main column. Using these types of instruments 5 to 10 samples can be taken per hour during a 24-hour day.

Portable gas chromatographs that are less expensive than those described above are commercially available for monitoring VCM, but require an attendant. Both FID and ECD are available with these instruments with a reported sensitivity of 0.1 ppm VCM.

The interim procedure[23] has been very useful in obtaining preliminary data and defining the magnitude of the problem, however.

well defined studies should be undertaken to eliminate sources of errors and refine the procedures prior to standardization.

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5. ENVIRONMENTAL APPRAISAL

5.1 SOURCES

Current monomer processes are of four types:

1. acetylene plus hydrogen chloride;
2. direct chlorination of ethylene and dehydrochlorination;
3. balanced direct and oxychlorination of ethylene and dehydrochlorination;
4. oxychloriantion using oxygen instead of air, Current polymer processes are categorized as: suspension, emulsion, bulk, and solution. Thus eight basic processes are discussed.

This review is limited to existing commercial processes in the United States. There are two general methods for the production of vinyl chloride monomer. These are the acetylene hydrogen chloride reaction:

$$HC \equiv CH + HCl \longrightarrow H_2C = CHCl$$

and the thermal dehydrochlorination of 1,2-dichloroethane:

$$ClCH_2 - CH_2Cl \longrightarrow H_2C = CHCl + HCl$$

Vinyl chloride monomer (VCM) plants are integrated with an ethylene dichloride production unit in the second procedure. The overall processes differ primarily in the manner in which the ethylene dichloride is produced.

Nine producers operate a balanced plant in which ethylene is chlorinated by a mixture of hydrogen chloride (HCl) and air to produce ethylene dichloride. Part of the HCl used for this process is in the form of recycled products from the thermal dehydrochlorination of ethylene dichloride as shown above.

Three producers use an integrated process in which the ethylene dichloride is produced by the direct chlorination of ethylene. Hydrogen chloride is recovered from the dehydrochlorination step, but is not recycled into the process.

One producer uses the balanced oxychlorination process with the exception that oxygen is used for the oxychlorination reaction sequence. Two companies use acetylene as the starting material.

Polyvinyl chloride (PVC) is produced at thirty-seven sites at a total yearly rate of approximately 2.4 billion kg. There are four processes used to manufacture PVC:

1. suspension polymerization (78 percent of total production);
2. emulsion polymerization (12 percent of total production);
3. bulk polymerization (6 percent of total production); and
4. solution (4 percent of total production).

Emissions of gaseous vinyl chloride monomer (VCM) are known to occur at both VCM and PVC resin plants. This VCM is distributed into the atmosphere surrounding the emissions source in patterns that depend on the amount of VCM released, the nature of the plant area from which it is released, and meteorological conditions. VCM air concentrations which may occur as a result of such releases are of interest.

Data accumulated for this study show that annual production capacities are 2.42 billion kg of VCM and 2.15 billion kg of PVC resin (Table 5.1). Manufacturers operated at full capacity in 1974. On the basis of the analysis of the VCM emission data so far supplied to EPA by VCM and PVC producers, total VCM escaping to the atmosphere is on the order of 95 million kg per year. However, approximately 90 percent of the total VCM emitted comes from PVC polymer production facilities. This is shown in Table 5.1.

Table 5.1. U.S. VINYL CHLORIDE MONOMER AND POLYMER PRODUCTION AND EMISSIONS (1973)

Plant type	Production Kg X 10^6/yr	VCM Emitted Kg X 10^6/yr	VCM Emitted Percent of production
VCM	2432	6-7	0.2 - 0.4
PVC	2159	65-86	3 - 4

It is also important to note that while monomer plants emit less VCM per kg of product than polymer plants, this may partially be offset by the tendency for monomer plants to have larger production capacities than polymer plants. The net result is that the absolute VCM emissions levels from polymer plants are usually in the range of 2 to 5 times those of monomer plants.

Two additional features of the industry are significant in terms of potential VCM concentration levels in the atmosphere near plants. VCM plants are clustered primarily in areas along the Texas and Louisiana Gulf coast, and PVC plants tend to be located close to/or even adjacent to the VCM production site. This "clustering" of plants is greatest on the Gulf coast in the Pasadena-Deer Park, Texas region and in the Baton Rouge, Louisiana area.

VCM monomer producing companies are listed in Table 5.2.1.Included in this table are the companies and their geographical locations, population figures for adjacent communities and calculated VCM emissions levels. PVC polymer producers are similarly listed in Table 5 2.2.Table 5.2.3 shows the location of geographical clusters of VCM and PVC plants.

5.2 OVERVIEW OF PROCESSES

The following tabulation of producers of vinyl chloride monomer indicates published production capacity and vinyl chloride emissions by process and location. (Table 5.2.1 through 5.2.3)

Table 5.2.1 MONOMER PLANT EMISSION DATA

Company	Location	City Population [a]	Production Capacity	Emissions [b]	Type Process
			$kgx10^9/yr$	$kgx10^6/yr$	
Allied Chemical	Baton Rouge, La.	165,963 [c]	136	0.4	B [d]
American Chem.	Long Beach, Ca.	358,633 [e]	77	0.2	B
Continental Oil	Lake Charles, La	77,998	273	0.8	B
Dow Chemical	Freeport, Tex.	11,997 [f]	82	0.2	DC
"	Plaquemine, La.	7,739 [g]	155	0.5	DC
"	Oyster Creek, Tex.	[f]	364	1.1	B
Ethyl Corp.	Baton Rouge, La.	165,963 [c]	123	0.4	B
"	Pasadena, Tex.	89,277 [h]	68	0.2	DC [i]
B.F. Goodrich	Calvert City, Ky.	31,627 [j]	455	1.4	B
Monochem, Inc.	Geismar, La.	7,739	136	0.4	A [k]
P.P.G. Industries	Lake Charles, La.	77,998	136	0.4	B
"	Guayanilla, P.R.	---	261	0.8	-
Shell Chemical	Deer Park, Tex.	12,773 [h]	398	1.2	B
"	Norco, La.	---	318	0.9	B
Tenneco Chem.	Pasadena, Tex	89,277 [h]	114	0.4	A
TOTALS		1,096,984	3096	9.3	

(a) 1970 Census data

(b) Extrapolated figures based on estimated atmospheric emission loss of 0.3 per cent of VCM produced in monomer plants

(c) Baton Rouge Parrish (County) - 302,031

(d) Balanced (B) - combination of direct chlorination (DC) and oxychlorination process in which the hydrogen chloride produced in cracking is recycled to the oxychlorination process.

(e) Los Angeles County - 7,032,075

(f) Brazoria County - 108,312

(g) Plaquemine Parrish (County) - 25,225

(h) Harris County - 1,741,912

(i) Direct Chlorination (DC)

(j) Population given is for Paducah, Ky.

(k) Acetylene (A)

Table 5.2.2. PVC POLYMER PLANT VCM EMISSIONS DATA

Company	Location	City population [a]	Type of process [b]	PVC capacity kg x 10^6/yr	VCM emissions [c] kg X 10^6/yr
Plastics Division Air Products & Chem., Inc.	Calvert City, Ky. Pensacola, Fla.	31,627 [d] 59,507	Suspension	59 23	2.2 0.9
American Chem. Corp. (Joint Venture-Altlantic Richfield Co. & Stauffer Chem. Co.)	Long Beach, Ca.	358,633 [e]	Suspension	57	2.3
Borden Chem. Division Borden, Inc.	Illiopolis, Ill. Leominster, Mass.	1,122 32,939	Suspension & Emulsion	129 [f]	5.2 [f]
Conoco Plastics Division Continental Oil Co.	Aberdeen, Miss. Oklahoma City, Okla.	6,157 366,481 [g]	Suspension & Emulsion	100 36	4.0 1.5
Diamond Shamrock Chemical Co. (Subsidiary Plastics Div.) Diamond Shamrock Corp.	Delaware City, Dela. Deer Park, Tex.	2,024 12,773 [h]	Suspension & Emulsion	113 [f]	4.5 [f]
(Industrial Chemical Div.) Ethyl Corp.	Baton Rouge, La.	165,963 [i]	Suspension & Emulsion	82	3.3
Chem./Plastics Division The Firestone Tire & Rubber Co.	Perryville, Md. Pottstown, Pa.	2,091 25,355	Suspension, Emulsion & Solution [5]	59 64 15	1.9 2.5 6.8
Chemical/Plastics Division The General Tire & Rubber Co.	Ashtabula, Ohio	24,313			
B.F. Goodrick Chemical Co. The B.F. Goodrich Co.	Long Beach, Ca. Henry, Ill. Louisville, Ky. Avon Lake, Ohio Pedricktown, N.J.	358,633 [e] 2,610 [j] 361,472 12,261 ---	Suspension, Emulsion, Bulk [20] & Solution [10]	57 57 125 57 59	2.3 2.3 5.0 2.3 2.4

Table 5.2.2 (Continued)

Company	Location	City population [a]	Type of process	PVC capacity kg X 10^6/yr	VCM emissions kg X 10^6/yr
Chemical Division The Goodyear Tire & Rubber Co.	Plaquemine, La. Niagra Falls, N.Y.	7,739 [k] 85,615	Suspension, Emulsion & Bulk 35	45 45	1.8 1.8
Great American Chemical Corp.	Fitchburg, Mass.	43,343	Suspension	18	0.7
Keysor-Century Corp.	Saugus, Ca.	--- e	Suspension	16	0.6
Monsanto Polymers & Petro-Chemicals Company Monsanto Company	Springfield, Mass.	163,905	Suspension & Emulsion	68	2.7
National Starch & Chemical Corp.	Meredosia, Ill.	1,178	Emulsion	5	0.2
Hooker Chemical Corp. (Subsidiary Ruco Div.) Occidental Petroleum Corp.	Burlington, N.J. Hicksville, N.Y.	11,991 [1] 48,075	Suspension & Bulk 70	82 5	3.3 0.2
Thompson Plastics Co. Div. Olin Corp.	Assonet, Mass.	---	Suspension	68	2.7
Pantasoto Co.	Passaic, N.J. Point Pleasant, W.Va.	55,124 6,122	Emulsion	120 [f]	2.2 [f]
Robintech, Inc.	Painsville, Ohio	16,536	Suspension	113	4.5
Plastics Division Stauffer Chemical Co.	Delaware City, Dela.	2,024	Suspension	73	2.9
Tenneco Plastics Division Tenneco Chemicals, Inc.	Burlington, N.J. Flemington, N.J. Pasadena, Texas	11,991 [1] 3,917 [h] 89,277 [h]	Suspension & Emulsion	75 27 136	3.0 1.1 5.4
Chemicals & Plastics Div. Union Carbide Corp.	Texas City, Tex. So. Charleston, W.Va.	38,908 16,333	Suspension & Solution 50	91 54	3.6 2.2

Table 5.2.2 continued

Footnotes

[f] Total for two plants

[g] Oklahoma County - 526,805

[h] Harris County - 1,741,912

[i] Baton Rouge Parrish (County) - 302,031

[j] Henry County - 53,217

[k] Plaquemines Parrish (County) - 25,225

[l] Burlington County - 323,132

Table 5.2.2 continued

Company	Location	City Population [a]	Type of Process [b]	PVC capacity kg X 10^6/yr	VCM emissions [c] kg X 10^6/yr
Uniroyal Chemicals, Inc. Uniroyal, Inc.	Painsville, Ohio	16,536	Suspension & Emulsion	14	2.5
			Subtotal	3,156	86.3
UNDER CONSTRUCTION					
Certeinteed Corp.	Lake Charles, La.	77,978	(unknown)	90	4
Georgia Pacific	Plaquemine, La.	7,739	"	90	4
Shintech	Oyster Creek, Tex.	11,997	"	110	5
			Subtotal	290	13
			TOTAL	2,446	99

Footnotes

[a] 1970 Census Data - Office Air Quality Programs' computer file.

[b] The statement on type of process is a preliminary one. Numbers in parenthesis indicate estimated production by that process in millions of pounds per year.

[c] Extrapolated figures in millions of kg per year (industry total 100 million kg/yr) based on estimated emission of 4.0 percent VCM during polymer production and recovery.

[d] Population given is for Paducah, Ky.

[e] Los Angeles County - 7,032,075

Table 5.2.3 CLUSTERS OF VINYL CHLORIDE EMISSIONS DO NOT QUOTE DRAFT

Company	Location	City population [a]	Capacity kg X 10^6/yr	Emissions [b] kg X 10^6/yr	Type process
Allied Chemical	Baton Rouge, La.	165,963 [c]	136	0.4	B [d]
Dow	Plaquemine, La.	7,739 [f]	154	0.5	DC
Ethyl Corp.	Baton Rouge, La.	165,963 [c]	122	0.4	B
Ethyl Corp. (Industrial Chem. Div.)	Baton Rouge, La.	165,963 [c]	82	3.3	Suspension
Georgia Pacific (under construction)	Plaquemine, La.	7,739 [f]	91	3.6	Unknown
The Goodyear Tire & Rubber Co. (Chemical Div.)	Plaquemine, La.	7,739 [f]	45	1.8	Suspension
Monochem, Inc.	Geismar, La.	7,739 [f]	136	0.4	A [k]
Area emissions				10.4	
Continental Oil	Lake Charles, La.	77,998	272	0.8	B
P.P.G. Industries	Lake Charles, La.	77,998	136	0.4	B
Shell Chemical	Narco, La.	---	38	0.9	B
Certainteed Corp. (under construction)	Lake Charles, La.	77,998	91	3.6	(unknown)
Area emissions				5.7	
Diamond Shamrock Corp., Diamond Shamrock Chem. Co. (Subsidiary Plastics Div.)	Deer Park, Tex.	12,773 [g]	113	9.5	Suspension & Emulsion
Ethyl Corp.	Pasadena, Tex.	89,277 [g]	68	0.2	DC [h]

Table 5.2.3 (CONTINUED)

Company	Location	City population	Capacity kg X 10^6/yr	Emissions[b] kg X 10^6/yr	Type process
Shell Chemical	Deer Park, Tex.	12,773 [g]	397	1.2	B
Tenneco Chem.	Pasadena, Tex.	89,277 [g]	113	0.4	A [j]
Union Carbide Corp., Chemicals & Plastics Div.	Texas City, Tex.	38,908	91	3.6	Suspended
Area emissions				9.9	
Dow Chemical	Freeport, Tex.	11,997 [e]	82	0.2	DC
Dow	Oyster Creek, Tex.	11,997 [e]	363	1.1	B
Shintech	Oyster Creek, Tex.	11,997 [e]	113	4.5	Unknown
Area emissions				5.9	

(a) 1970 Census data

(b) Extrapolated figures based on estimated atmospheric emission loss of 0.3 per cent of VCM produced in monomer plants

Extrapolated figures in millions of kg per year (industry total 100 million kg/yr. Yr^{-1}) based on estimated emission of 4.0 percent VCM during polymer production and recovery.

(c) Baton Rouge Parrish (County) - 302,031

(d) Balanced (B) - combination of direct chlorination and oxychlorination process in which the hydrogen chloride produced in cracking is recycled to the oxychlorination process.

(e) Brazoria County - 108,312

(f) Plaquemine Parrish (County) - 25,225

(g) Harris County - 1,741,912

(h) Direct Chlorination (DC)

(i) Acetylene (A)

REFERENCES

1. Bureau of Census data, Monitoring and Analysis Division, OAQPS computer files, 1970.

2. Carpenter, B.H. Vinyl Chloride - An Assessment of Emissions, Control Techniques and Cost. Research Triangle Institute Report for CSL, NERC, RTP, July, 1974.

3. Personal Communications between Industry representatives responding to OAQPS Section 114 letters to EPA personnel, May 1974.

5.3 CONCENTRATIONS

A paucity of data exists concerning the concentration of vinyl chloride in ambient air. In view of the potential health hazard associated with VCM, a preliminary field study was initiated to obtain more extensive and reliable data in the area of industrial emission sources. The task of obtaining these data for air and water was assigned to the EPA Regional Offices. Interim procedures were established by EPA to insure comparability of the data. The initial data from these surveys will be reviewed in this section. Generally, it would appear that the Regions had varying degrees of resources and expertise in the area of air monitoring. In addition, the interim procedure was not followed religiously in some cases, making comparisons of data between regions difficult. Levels for residential areas are usually expressed in parts per million (ppm) VCM, the concentration of VCM occurring in residential areas not not known with certainty at the present time but appear to be below 1 ppm - 90 percent of the time based upon the limited data presently available.

5.3.1 Air

Most of the available data are from instantaneous samples. Because of the discontinuous nature of the chemical process and emissions, the values were expected to, and in fact did, range widely. Values were as high as 33 and 3.4 ppm at distances of 0.3 to 3 miles respectively from emission sources.

5.3.1.1 Plant I

5.3.1.1.1 Grab samples--Summary data from the samples are tabulated in Table 5.3.1 The distance from the center of the plant to the sites is shown in the second column. Samples taken at site

Table 5.3.1 CONCENTRATION OF VCM IN GRAB SAMPLES TAKEN AT PLANT

Plant I - Grab Samples

Site	Distance km		No. of Samples	Maximum ppm	Average[a] ppm	No. >1 ppm[b]
A	0.2	0.3	17	6.0	0.52	2
B	0.1	0.2	16	0.30	0.06	0
C	0.2	0.3	9	0.22	0.06	0
D	0.1	0.2	9	0.9	0.15	0
E	0.4	0.6	11	0.6	0.14	0
F	0.4	0.6	9	0.24	0.09	0
G	0.5	0.8	8	-	0.03	0
H	0.5	0.8	10	-	0.03	0
I	0.7	1.1	12	0.40	0.05	0
J	1.0	1.6	8	-	0.03	0
K	1.2	1.9	7	0.24	0.06	0
L	3.0	9.8	8	-	0.03	0
M	0.6	1.0	6	-	0.03	0
N	0.6	1.0	4	-	0.03	0
O	0.7	1.1	5	-	0.03	0
P	0.5	0.8	6	0.32	0.11	0
T	0.1	0.2	1	-	0.03	0
U	0	0	2	0.24	0.22	0
V	0	0	1	-	0.03	0
W	0.1	0.2	3	2.6	1.48	2
X	0.2	0.3	1	0.16	0.17	0
Y	0	0	1	5.7	6.15	1
Z	0.2	0.3	1	-	0.03	0

[a]Values corrected to standard temperature of 25°C.

[b]Frequency of VCM measured concentrations above 1 ppm.

A through P were collected at two hour intervals with Tedlar (R) bags or syringes. The remaining sampling sites were those where detectable odors existed. Columns 3, 4 and 5 list the number of samples collected and analyzed, the maximum concentration of VCM found and the average at each site. The last column was included to show the frequency that the concentration of VC exceeded 1 ppm. Over 90 percent of the values obtained were below minimum detectable values, 0.06 ppm. Figure 5.3.1 is a histogram of the observed data above the detectable level. In calculating the mean values, below detectable concentrations were arbitrorily given values of 0.03 ppm, one-half the minimum detectable level. Excluding the random samples, the individual values range from below detectable to 6 ppm.

5.3.1.1.2 Twenty four hour samples- Table 5.3.2 shows the average values of VCM in a 24-hour period that were collected on charcoal scrubbers. All data shown in the Table were corrected to ambient air standard conditions of 25°C and 1 atmosphere. On May 10, the average value at site A exceeded 1 ppm. The report indicates, however, that although site A was 0.2 mile from the center of the plant, it may actually have been closer to the major source of PVC emissions.

5.3.1.2 Plant IV--At the present time only the data from the initial study and summary data are available. Table 5.3.3 shows the result of the data collected in March. Only three values exceeded 1 ppm, the highest was 2.2 ppm. The frequency distribution of these values is shown in Figure 5.3.2. The summary of data collected in May around this plant are tabulated in Table 5.3.4. One

Table 5.3.2 CONCENTRATION OF VCM MEASURED IN INTEGRATED SAMPLES COLLECTED BY CHARCOAL ABSORBER AT PLANT I, ppm

Site	Date		
	5/9/74	5/10/74	5/13/74
Site			
A	0.021	1.15	0.165
B	0	0.005	0.020
C	0	0.009	0.029
D	0.141	0.010	0.090

Table 5.3.3. CONCENTRATIONS OF VCM IN GRAB SAMPLES TAKEN AT PLANT IV IN MARCH 1974

Site	Distance, km	Number of Samples	Maximum (ppm)	Mean, ppm	No. 1 ppm
A	0	6	2.2	0.84	2
B	0.6	3	0.58	0.40	0
C	0.6	4	1.26	0.33	1
D	0.6	6	0.29	0.12	0
E	0.8	3	0.24	0.16	0
F	0.8	15	0.39	<0.17	0
G	0.8	2	-	<0.17	0
H	0.5	1	-	<0.17	0
I	1.3	1	-	<0.17	0
J	1.0	1	-	<0.17	0
K	1.0	2	-	<0.17	0
L	1.3	1	-	<0.17	0
M	4.8	2	-	<0.17	0
N	1.0	1	-	<0.17	0

TABLE 5.3.3. CONCENTRATION OF VCM IN GRAB SAMPLE COLLECTED AT PLANT II IN MAY 1974

Site	Distance, km	Number of Samples	Maximum, ppm	Mean, ppm
A	0	6	1.7	0.33
B	0.6	21	5.6	1.6
C	0.6	21	5.8	0.71
D	0.6	19	2.8	0.54
E	0.8	2	0.10	0.07
H	0.5	3	1.2	0.50
I	1.3	2	1.6	1.00
L	1.3	2	BD	BD
N	1.0	1	BD	BD
P	0.6	8	0.08	0.06
Q	0.8	12	1.7	0.54
R	0.5	83	33.0	3.15
S	0.6	1	1.2	1.20
T	1.0	3	0.57	0.21
U	1.0	3	BD	BD
V	0.2	1	BD	BD

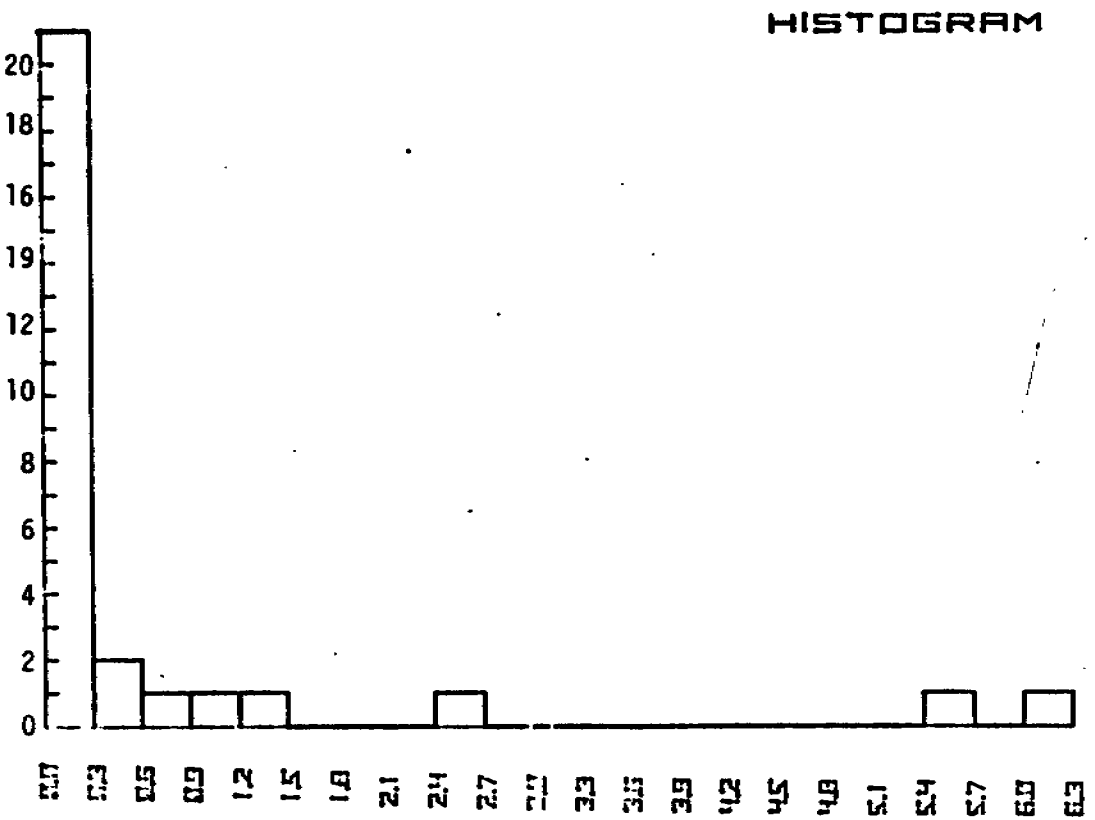

Figure 5.3.1. Histogram showing frequency distribution of VCM grab samples concentrations at Plant I.

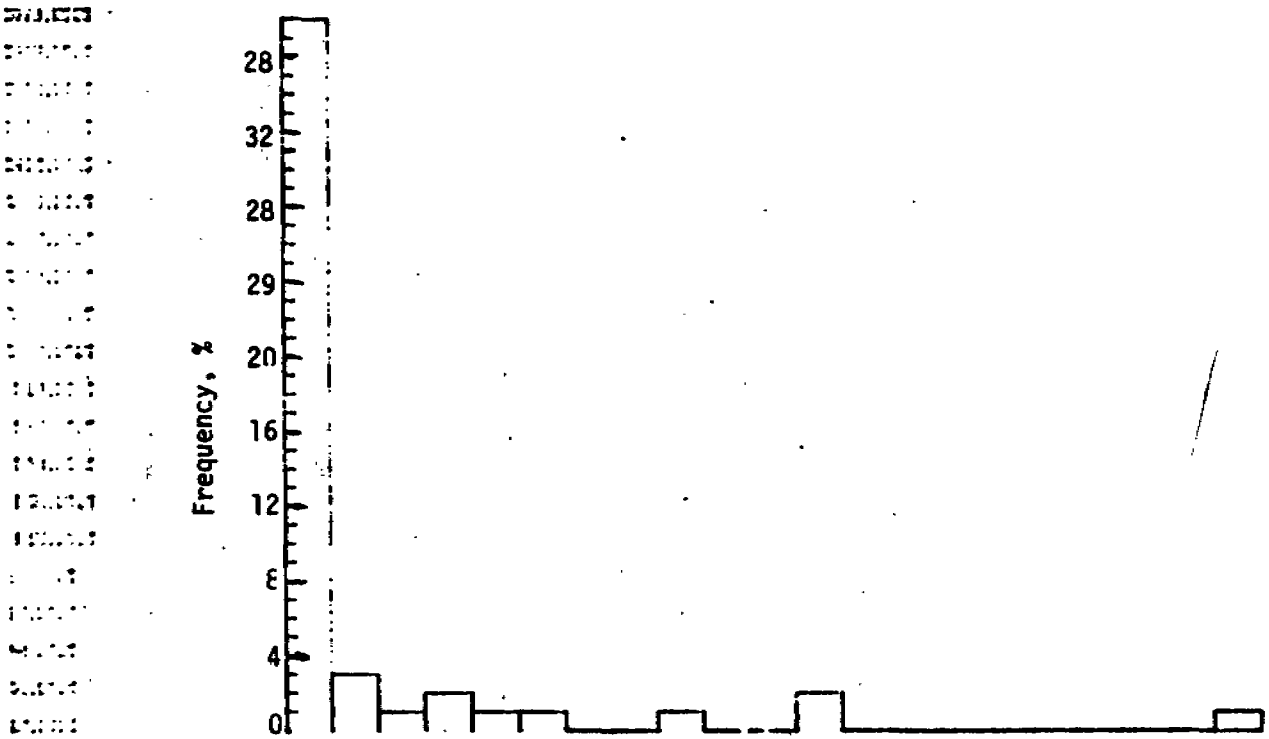

Figure 5.3.2. Histogram showing frequency Distribution of VCM Grab Sample Concentration for Plant IV ($\bar{X}$ 0.33, σ 0.40).

instantaneous value of 33 ppm was observed at a distance of 0.5 km from the plant, and one mean value at site B exceeded 1 ppm. The data from the 24-hour integrated samples indicated the highest value to be 0.55 ppm (Table 5.3.5.

5.2.1.3 Plant VI--Here again, only summary data are available. Table 5.3.6 and Figure 5.3.3. show the observed values at various distances from the plant, and the frequency distribution of these data. Only three values exceeded 1 ppm. The range of concentration at the property line was from below detectable levels to 7.8 ppm.

5.2.1.4 Plant IX--The most complete report was provided by Region IX which was prepared in cooperation with the National Field Investigating Center - Denver. However, the data (Table 5.3.7) provided were from samples on charcoal and are 10 minute averages instead of instantaneous samples; and hence this data is not comparable with the preceding. Under these conditions, values as high as 3.4 ppm were found at a distance of 4.8 km from the plant. Only 12 of the 180 determinations exceeded the 1 ppm level. The overall mean value calculated was 0.24 $\pm$ 0.44 ppm.

5.3.2 Summary

Since a great deal of latitude was excercised in implementing the prescribed procedures, it is difficult to compare the data from different plants. Based upon the available data, peak values as high as 33 ppm might be expected in the vicinity of VCM emission sources. All values obtained are expected to be biased negatively.

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Table 5.3.5. CONCENTRATION OF VCM IN 24-HOUR AVERAGE SAMPLES

Site	Distance, km	VCM, ppm
MSD	0.6	0.16
NFL	0.6	0.07
SOP	0.3	0.55
DPT	0.2	0.10
CP	1.0	0.01

Table 5.3.6. CONCENTRATION OF VCM IN GRAB SAMPLES TAKEN AT PLANT VI, ppm

Date	0	0.8	1.2	1.6	3.2	4.0	4.8
5/7/79	2.069	0.001	BD[a]	0.002	0.002		0.002
	0.045	0.002					0.001
	7.814						
5/8	3.218		0.003	0.002	0.003		
	0.666	0.356					
	0.003	BD[a]					
5/9	0.095		BD[a]		0.023	BD[a]	0.000
	0.078		0.168		0.168		
			0.001		0.181		
Maximum Value	7.8	0.34	0.17	0.002	0.18	BD[a]	0.002

[a]Below detection.

TABLE 5.3.7.

PLANT IX - Integrated - 10 Minute Average as Charcoal Samples

Run number	Station Number / Distance from source, km														
	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
	2.4	1.8	2.4	4.5	4.3	5.0	5.0	1.6	3.1	1.1	1.4	0.8	1.0	1.9	2.1
70	0.05	0.15	0.24	0.23	0.25	0.25	0.06	0.05	0.05	0.11	0.11	0.21	0.05	0.11	0.03
71	0.53	0.06	0.04	0.06	0.31	0.14	<0.05	0.21	0.40	0.02	0.05	0.02	0.05	0.06	0.04
72	0.03	0.29	0.05	0.04	0.08	0.08	0.33	0.03	0.10	0.08	0.04	0.02	0.03	1.0	0.10
73	0.10	0.11	0.03	0.04	0.06	0.13	0.29	2.7	0.03	0.37	0.26	0.16	0.34	0.09	0.01
74	0.23	0.15	0.16	0.04	0.12	0.45	0.21	0.05	0.04	2.1	0.03	0.03	0.11	1.3	0.03
75	0.05	0.43	0.03	0.05	0.10	0.16	3.4	0.23	0.16	0.05	0.07	0.03	0.25	0.05	0.09
76	0.03	0.04	0.02	0.02	0.20	0.05	0.06	0.03	0.06	0.06	0.22	1.1	0.15	0.07	0.48
77	0.10	0.19	0.29	0.11	0.55	0.04	0.53	0.98	0.16	0.36	0.45	0.07	0.04	0.05	0.15
78	0.04	0.24	0.03	0.32	0.08	1.4	0.69	0.31	0.33	1.1	0.08	1.0	0.50	0.14	0.03
79	0.07	0.10	0.85	0.18	0.26	0.17	0.08	0.12	0.05	0.02	0.24	0.08	0.03	0.02	0.06
80	0.09	0.11	0.05	0.08	0.07	0.03	0.02	0.03	0.05	0.02	0.03	0.07	0.05	0.03	0.07
81	0.03	0.24	0.06	0.25	1.2	0.02	0.10	0.04	1.7	0.06	0.04	0.84	0.15	1.1	0.33
Average	0.12	0.18	0.16	0.12	0.28	0.25	0.53	0.41	0.26	0.36	0.14	0.30	0.15	0.33	0.12
Maximum	0.53	0.43	0.85	0.32	1.2	1.4	3.4	2.7	1.7	2.1	0.45	1.1	0.50	1.3	0.48
X> 1ppm	0	0	0	0	1	1	1	1	1	2	0	2	0	3	0

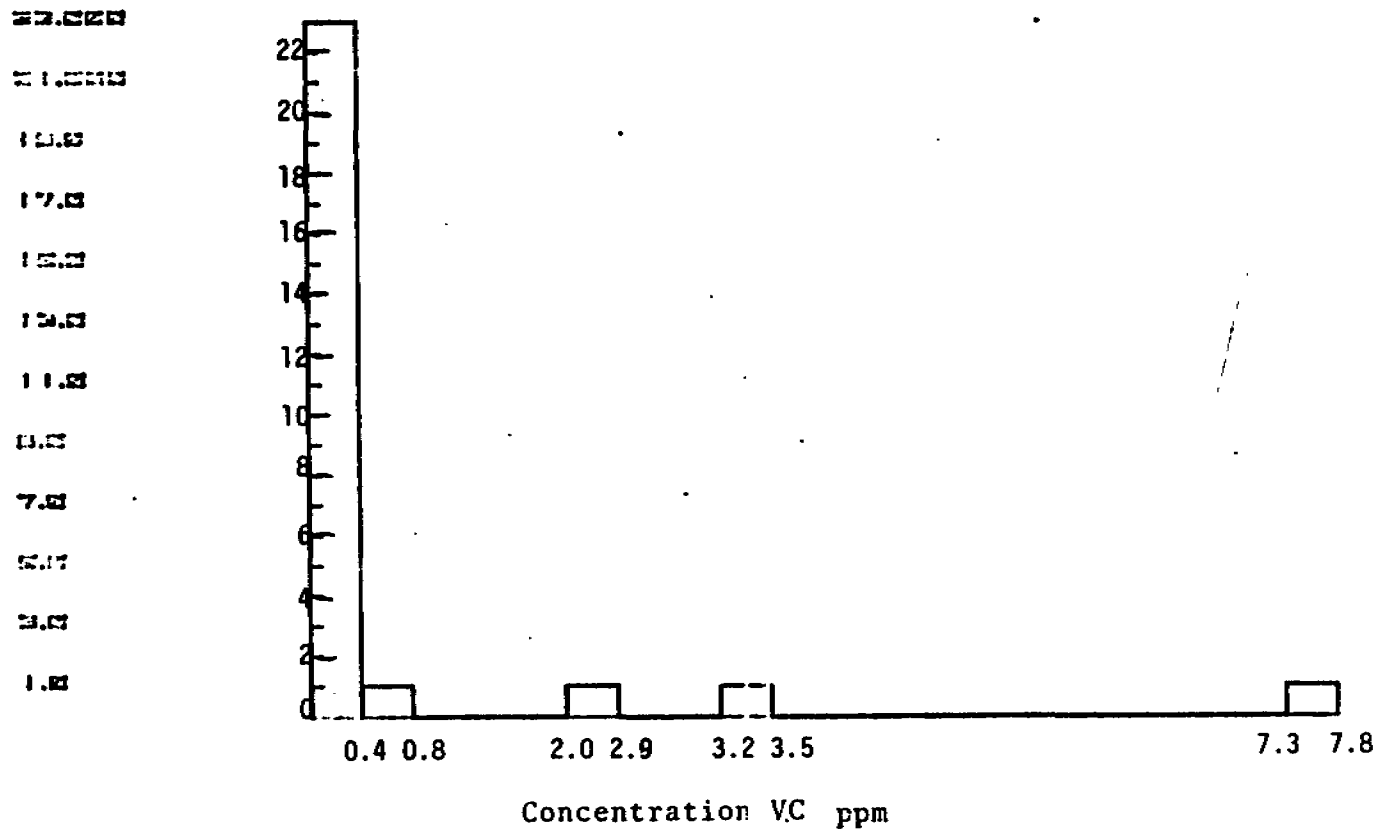

Figure 5.3.5. Histogram of Frequency Distribution of VCM Grab Sample Concentrations at Plant VI. ($\bar{X}$ 0.5, σ 0.40)

Grab samples are expected to lose quantities of VCM due to continuing reaction in the sampling container, wall loses, leaks, etc. Indication of VCM losses in these containers range from 0 to 10 percent per day. Losses of VCM while using charcoal are expected to be larger than in the containers. Collection efficiency and recoveries have not been definitively established. Preliminary data indicate recoveries of 71 to 76 percent when extraction by CS_2 is used to recover the VCM from charcoal. For 7 data points in which samples were collected in parallel and analyzed by two different laboratories, the values disagreed markedly. The relative standard deviation about the mean ranged from 5 to 140 percent.

Table 5.3.8. CONCENTRATION OF VCM MEASURED IN INTEGRATED 24-HOUR SAMPLES COLLECTED BY CHARCOAL ABSORBER AT PLANT IX, ppm

Distance, km	Date		
	5/7/74	5/8/74	5/9/74
1.1	0.08[a]	0.07[a]	0.10[a]
1.3	0.08	0.08	0.05
3.1	---	0.06	0.05
4.3	---	0.06	0.05
4.5	0.27	0.65	0.27
5.3	0.07	0.04	0.05

[a]12-Hour Samples

5.4 ESTIMATES OF AIR QUALITY CONCENTRATIONS

Estimates of vinyl chloride concentrations downwind of two plant sites were made using available emission estimates and reasonable meteorological conditions. The estimates were made using Gaussian dispersion techniques given in EPA's Workbook of Atmospheric Dispersion Estimates.[1] Concentration estimates are for 1-hour averaging times. Considering possible errors in emissions and dispersion uncertainties, the estimates may be expected to be within a factor of 3 or 4 of concentrations that would be measured under the same meteorological conditions at the same receptors with accurate sampling equipment. Table 5.14 shows the results of the estimates for four different emission conditions. Wind speed was held constant at 2 m/sec for all calculations. Since concentration is inversely proportional to wind speed, a higher wind speed would decrease the estimates; a lower wind speed would increase the concentrations estimates. Wind speeds lower than 2 m/sec occur fairly often, on the order of 3 to 15 percent of the time, at most locations. Three different atmospheric stabilities were considered. D, or neutral, stability occurs during day or night when cloudy skies prevail. This stability also occurs during the transition from unstable daytime conditions to stable nightime conditions and vice versa. E, slightly stable, and F, moderately stable, both occur at night with clear skies and light winds. These three meteorological conditions can be expected to occur during quite a number of hours in a given year.

Receptor locations in these model calculations were placed at positions downwind of the approximate center of the sources and off the plant property.

For plant A, a computation was made considering the emissions from 5 point sources of varying heights and from one area source. These sources are all located within 200 meters of each other. From the top portion of Table 5.4.1, it is seen that the predicted maximum hourly concentrations do not differ greatly for the three stabilities, and are the highest, 4 ppm, for F stability (moderately stable). Maximum 24-hour concentrations would be much lower.

Concentrations resulting from this plant were also estimated when a reactor is aborted and over 2270 kg of VCM is vented to the atmosphere in about 10 minutes. Venting such as this would occur approximately 20 times each year in a PVC plant. Other emissions were assumed to remain the same as in the above calculation. Under these conditions a maximum hourly concentration of 29 ppm was predicted to occur under D stability at 400 meters. Since the other sources contribute less than 3 ppm at this point, the vented release contributes about 26 ppm at this point. Since the release occurs over only a 10 minute period, a much higher concentration with instantaneous peaks 5 to 10 times this concentration, 130-260 ppm, might be expected, based on these calculations, to occur at this receptor as the pollutant cloud passes. Concentrations at least 5 times higher, 133 ppm, might occur over a 6 to 10 minute averaging time at this receptor according to these estimates. Beyond 5.0 km the impact of a spill would be minimal. For both the spill and non-spill situations, the populations most affected would be those residing within about 2 km of the plant.

Table 5.4.1. CALCULATED 1-HOUR AVERAGE CONCENTRATIONS OF VINYL CHLORIDE AT SELECTED DOWNWIND DISTANCES FROM A PLANT WITH MULTIPLE EMISSION SOURCES

Distance from plant, km	Concentration, ppm[a,b]					
	Stability class[c]		Stability class[d]		Stability class[e]	
	No spill	With spill[f]	No spill	With spill[f]	No spill	With spill[f]
0.25	3.5	18.2	3.8	3.8	4.0	4.0
0.4	2.9	29.3	3.4	4.4	3.9	3.9
0.5	2.6	28.2	3.2	6.1	3.7	4.0
0.8	1.7	19.4	2.5	10.9	3.2	7.1
1.0	1.4	14.9	2.1	11.8	3.0	9.5
2.0	0.6	6.0	1.1	8.2	1.9	11.8
3.0	0.4	3.4	0.7	5.4	1.3	9.3
5.0	0.2	1.6	0.3	3.0	0.8	5.9

[a]Emission conditions:

Source type	Emission rate, g/sec	Height of emission, m
Point	18.9	22.9
Point	0.63	15.2
Point	6.3	7.6
Point	8.8	30.5
Point	0.5	38.1
Area[g]	44.1	6[g]
Spill[f]	3783.3[f]	15.2

[b]All calculations assume 2.0 m/sec windspeed.

[c]Neutral conditions

[d]Slightly stable.

[e]Moderately stable.

[f]Spill of 2270 kg of vinyl chloride released in 10 minutes at a height of 15.2 meters at 338°K (65°C).

[g]Emissions from a building 110 by 170 m through vents and windows about 6 m from the ground.

Table 5.4.2. CALCULATED 1-HOUR AVERAGE CONCENTRATIONS OF VCM AT SELECTED DOWNWIND DISTANCES FROM A PLANTS WITH MULTIPLE EMISSION SOURCES

Distance downwind (Km)	Concentration, ppm[a]					
	Stability D		Stability E		Stability F	
	Average emissions[b]	Peak emissions[c]	Average emissions[b]	Peak emissions[c]	Average emissions[b]	Peak emissions[c]
0.2	2.2	2.8	2.8	3.3	3.1	3.6
0.3	1.8	2.4	2.5	3.0	3.1	3.7
0.4	1.6	2.2	2.2	2.7	2.9	3.5
0.5	1.4	2.1	1.9	2.4	2.7	3.2
0.8	1.0	1.7	1.5	2.1	2.2	2.7
1.0	0.8	1.5	1.3	2.0	2.0	2.4
2.0	0.4	0.8	0.7	1.3	1.2	1.9
3.0	0.3	0.5	0.5	0.9	0.9	1.5
4.0	0.2	0.3	0.3	0.7	0.7	1.3
5.0	0.1	0.3	0.3	0.5	0.5	1.0
10.0	<0.1	0.1	0.1	0.2	0.2	0.5
15.0	<0.1	<0.1	<0.1	0.2	0.2	0.3
20.0	<0.1	<0.1	<0.1	<0.1	0.1	0.2

[a]All calculations assume 2.0 m/sec wind speed

[b]Average emissions:
Point source -- 24.0 g/sec. at 33.5 m.
Area source 1 -- 21.4 g/sec from 150 by 150 meter building. Assume emission at 6m.
Area source 2 -- 14.4 g/sec. from 180 by 15 meter building. Assume emission at 6m.

[c]Peak emissions:
Point source -- 90.5 g/sec. at 33.5m.
Area source 1 -- Same as under average emissions.
Area source 2 -- Same as under average emissions plus a 2 minute spill of 24,000g. (2000g/sec).

For Plant B, one point source and two area sources were considered under two differenct conditions, average emissions and peak emissions. Three emission sources are assumed located within 300 meters of each other in this calculation. In this case the maximum concentrations are not increased greatly by an increase of a factor of three in the emissions from the elevated point and/or by a 2 minute spill from the area source. However, note that the concentrations are nearly doubled at greater distances downwind. For Plant B the maximal concentration, 3.7 ppm, is almost the same as that from Plant A under normal conditions, 4 ppm.

REFERENCES

1. Turner, D.B. Workbook of Atmospheric Dispersion Estimates. EPA, Research Triangle Park, N.C. Publ. No. AP-26, 84p, 1970.

5.5 TRANSFORMATION, TRANSPORT, AND REMOVAL

No results on the reactions and rates of disappearance of vinyl chloride from the ambient atmosphere are available at present. Limited laboratory studies on the stability and persistence of vinyl chloride in air have, however, been completed. In addition measurements recently reported on vinyl chloride in water and sludge indicate that vinyl chloride dumped into aqueous media are probably lost to the air relatively rapidly.

Vinyl chloride vapor concentrations in containers of various materials appear to be essentially constant over periods of many days. The peak absorption of vinyl chloride in the ultraviolet region is very far below the solar cutoff around 290 nm so VCM would not undergo reaction in sunlight in the absence of other reactive chemical species. When irradiated with simulated solar radiation in the presence of nitrogen oxides (nitric oxide and nitrogen dioxide), vinyl chloride in the parts per million concentration range does react to form a variety of products. The available results indicate a rate of reaction of about 8 to 10 percent per hour for vinyl chloride. The reaction products identified include ozone, nitrogen dioxide, carbon monoxide, formaldehyde, formic acid, formyl chloride and hydrogen chloride. Several of these products are very irritating.

Although vinyl chloride would disappear significantly in traveling over longer distances, the conversions anticipated within a few kilometers downwind of vinyl chloride emission sources would be small. No mechanism is presently known for removal of vinyl chloride from the air during the nighttime hours. Biological sinks such as microbiological removal in soil may be of significance in depletion of vinyl chloride over long time periods, but such sinks would not be expected to be important in terms of urban scale transport of vinyl chloride. Thus, for a first approximation, vinyl chloride in the immediate vicinity of vinyl chloride emission sources can be considered a stable pollutant. The usual meteorological dispersion equations could thus be applied to approximate concentrations in the vicinity of emission sources. Because of strong radiation inversions at night during the fall and winter build-up of vinyl chloride from emission sources might be of particular concern during such periods.

The noxious gases which are products of vinyl chloride reactions (and possibly also from other chlorinated chemicals in industrial production) should not be ignored. In areas with large industrial activities involving large volume production of these chemicals, such products may contribute appreciably to eye, nose, throat and lung irritation, particularly on sunny days.

6. ENVIRONMENTAL EXPOSURE AND RECEPTOR RISK

Human exposure to vinyl chloride may occur from air inhalation, from consumption of food, from intake of water containing vinyl chloride, and from skin contact. The data available suggest that the airborne exposure route in general represents the greatest source of vinyl chloride intake for the population. The highest exposures to vinyl chloride occur in occupational situations where the vinyl chloride is manufactured and where the vinyl chloride monomer, a gas at room temperature and atmospheric pressure, is converted to a polymer. Workers involved in the polymerization process and in the fabrication of PVC into end products may be exposed not only to vinyl chloride in the gaseous phase but may also inhale PVC dusts containing entrapped vinyl chloride monomer. In this regard PVC particles containing vinyl chloride may be deposited in tissues.[1] To date there is not adequate information on general or occupational population exposure to PVC particles in the air.

Peak exposures to vinyl chloride in occupational situations may at times in the past have exceeded 1,000 ppm as for example during reactor cleaning operations,[2] although the highest time weighted average exposures were probably in the 250-500 ppm range.[3,4] The threshold limit value for vinyl chloride was at one time set at 500 ppm based upon its narcotic properties. After reports of liver damage due to vinyl chloride at exposures below 500 ppm were available the TLV was reduced to a 200 ppm time weighted average exposure for a forty-hour work week, with a 500 ppm ceiling for

peak exposures.[5,6] When it became evident from animal studies that vinyl chloride produced angiosarcoma of the liver at exposures as low as 250 ppm, and when cases of liver angiosarcoma were reported from workers in PVC production plants, an emergency ceiling TLV of 50 ppm was established and a recommendation to set a permanent standard at a no detectable limit based upon an analytical procedure capable of detecting vinyl chloride at concentrations of 1 ppm was made by the Department of Labor.[6] That recommendation has recently been modified and a permanent standard promulgated which calls for a maximum 8-hour worker exposure to vinyl chloride of 1 ppm with peak 15 minute exposures not to exceed 5 ppm. Since establishment of the 50 ppm emergency standard additional animal studies have shown vinyl chloride to be a carcinogen in experimental animals at 50 ppm exposure levels.[6,7] These data are reviewed more fully in the following sections.

Among the general population not involved directly in VC/PVC manufacture and product fabrication, the greatest sources of vinyl chloride exposure are estimated to be or to have been from aerosol products containing vinyl chloride propellants and from atmospheric emissions in the vicinity of industrial sources. Studies on vinyl chloride aerosols used in home situations indicate that peak exposures in excess of 100 ppm can occur.[8] Time weighted average air exposures to vinyl chloride in aerosol products would, of course, depend upon the frequency and conditions under which these products were used. To date over 100 aerosol products have been identified which either contained or currently contain vinyl chloride.

For populations residing in the vicinity of industrial sources preliminary date, described earlier, show peak exposure of 33 ppm and 24-hour samples as high as 1-2 ppm. Over 90% of samples, both peak and 24-hour measurements, were below 1 ppm.[9] It should be noted that the

risk to health may be related to the exposure pattern to vinyl chloride, i.e. intermittent peaks, a 40-hour exposure each work week or a continuous low level exposure.

Vinyl chloride concentrations of 2-3 ppm and at times higher have been recorded from manufacturing plant effluents, although it is unlikely that such contamination would persist in water downstream which might be used for drinking purposes, due to the tendency for vinyl chloride to escape from water into the air.[9] Water contamination with vinyl chloride from PVC piping may be a problem although available data do not indicate this to be the case. To date, there is no indication that drinking water contains detectable levels of vinyl chloride.[9] Food, either beverages or solids packaged in PVC containers, may contain vinyl chloride as a result of leaching, but the full extent of such a potential problem is at present unknown. A World Health Organization Report tentatively estimates that human intake of vinyl chloride, based upon a limited range of food is on the order of 1 µg per person per day.[11]

For the general population, it is impossible to quantitate the relative importance of various vinyl chloride exposure sources on an individual basis based upon current data. However, if the assumptions regarding levels of contamination are correct, the relative importance of these sources can be estimated. This estimate and the assumptions in these calculations are shown in Table 6.1.1.Conclusions drawn from this analysis are, of course, dependent upon the assumptions which are made. These estimates assume equal absorption of vinyl chloride from food and water in the gastrointestinal tract compared to vinyl chloride absorbed by the lungs from the air.

Table 6.1.1 RELATIVE IMPORTANCE OF VINYL CHLORIDE SOURCES FOR THE GENERAL ADULT POPULATION (mg VCM)

Food[1]	Water[2]	Air[3]	Total
0.002	--	3.0	3.002

[1]Assume 2 Kg ingested daily containing an average of 0.001 ppm VCH by weight resulting in an intake of 2 µg/day. A World Health Organization Report estimates the levels of vinyl chloride in food may be on the order of 1 microgram per person, per day, based upon tentative calculations from a limited range of foods."

[2]Assume 2 liters ingested daily containing no detectable levels of VCM. To date there is no indication that drinking water contains detectable levels of vinyl chloride.

[3]Assume inhalation of 20 m^3 per day containing 0.05 ppm vinyl chloride by volume.

This may or may not be true. Based upon these calculations, it is evident that the airborne source, in general, can be considered the most important route of exposure to this substance among the population.

Specification of the risk to health among the general population associated with the given airborne exposure to vinyl chloride is extremely difficult in large part due to the lack of information regarding responses to vinyl chloride at ambient dose levels in both animals and man. Further, the data available, regarding adverse effects attributable to vinyl chloride in man do not include adequate measures of exposure which may have been responsible for such damage.

In considering the risk to human health from vinyl chloride exposure in the population, it is important to keep in mind that angiosarcoma of the liver, though an invariably fatal disease, is not necessarily the most significant health effect associated with vinyl chloride. Other cancers may also be involved and non-malignant damage to the liver may affect a far greater proportion of the exposed population than those who develop angiosarcoma. To date angiosarcoma of the liver has been considered an extremely rare disease among the general population. In a survey by the American Cancer Society only one case of angiosarcoma

of the liver was recorded among 78,000 deaths.[12] However, the possibility that the frequency of this disorder has been greatly underestimated must be considered. Shown in Table 6.1.2 are the results of several studies examining the frequency of liver angiosarcoma among workers exposed to vinyl chloride.

Table 6.1.2

FREQUENCY OF LIVER ANGIOSARCOMA
AMONG DECEASED VINYL CHLORIDE WORKERS[13-16]

Number of Deaths		Reported Frequency of Liver Angiosarcoma	
		Number	Percent
a[13]	161	5	3.1
b[14]	24	3	12.5
c[15]	20	-	-
d[16]	109	6	5.5
Total	314	14	4.5

While it is likely that these reported cases of liver angiosarcoma occurred among workers exposed to levels of vinyl chloride many times greater than that normally found in the ambient air, it is also noteworthy that compared to the general population (1 case in 78,000) the relative risk of developing liver angiosarcoma among those exposed individuals by combining all these data is estimated to be approximately 3,000 times greater. Such a relative risk represents a striking

statistically significant difference ($p << 0.01$) in the frequency of liver angiosarcoma among those exposed to high levels of vinyl chloride compared to those in the general population exposed to much lower levels.

In attempting to assess trends in incidence of liver angiosarcoma among the population, it is important to recognize that other chemicals besides vinyl chloride may be contributing to such a phenomenon. Included in such a list would be materials with similar chemical structures to vinyl chloride as well as arsenicals and thorotrast, both of which have already been associated with angiosarcoma of the liver.[17-18]

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7.1 TOXICOLOGY

7.1.1 Introduction

The effects associated with vinyl chloride exposure include narcosis associated with acute exposure, and liver and low grade kidney damage similar to that associated with other halogenated aliphatic hydrocarbons. Acroosteolysis has also been observed among workers exposed to vinyl chloride. This disorder is characterized by degeneration of bones in the fingers and has been associated primarily with direct contact with polymerized material (PVC) and high levels of gaseous monomeric vinyl chloride.[1] This response is unique among the occupational hazards resulting from exposure to the aliphatic chlorohydrocarbons. The recent discovery that vinyl chloride induces carcinogenic changes in experimental animals and the appearance of liver angiosarcoma among PVC workers also appears to be a response to vinyl chloride exposure.[2-7] Although there has been no systematic quanitative assessment of the toxicity of the many halogenated hydrocarbons, vinyl chloride has until recently been considered one of the least toxic of the aliphatic chlorohydrocarbon chemicals.[8a]

Carcinogenic activity of vinyl chloride has been confirmed in several species of experimental animals and associated with both acute and chronic low level exposure when the experimental period was sufficient in time to permit tumors to appear.[2-5] The appearance of hepatic angiosarcoma, malignant lesion in the liver of experimental animals, and the discovery that this equally rare lesion in man is associated

with occupational exposure to vinyl chloride circumstances has served to underscore the predictive value of experimental toxicology. Questions have also been raised regarding the safety of other chemicals structurally related to vinyl chloride that traditionally have been considered of low order toxicity.[8] A literature review of the toxicology of vinyl chloride has recently been presented by Marsteller et al, 1974.[9] A summary of this information is presented in Appendix B. Since vinyl chloride is now a recognized chemical carcinogen that has been detected in the ambient air near monomer and polymer production facilities in the United States, its presence in the environment represents a potential public health hazard.

7.1.2 Acute Effects

The early experimental toxicology of vinyl chloride was limited to acute exposures. These early studies employed a variety of experimental animals and were limited to very short exposure periods. The results of these studies have been reviewed by von Oettingen,[11] Mastromatteo et al.[10] and more recently by Marsteller et al.[9] In general, these investigations suggested vinyl chloride was of low order acute toxicity, anesthetic in action, and had little capacity to cause injury to the liver or kidneys. The duration of these exposures ranged from minutes to hours. These observations led to consideration of vinyl chloride for use as a general anesthetic.[9] The anesthetic effects were often accompanied by

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cardiac irregularities with some suggestion of cardiac sensitization. The effective narcotic level in mice exposed to vinyl chloride for one minute ranged from 86,000 to 123,000 ppm. Approximately 170,000 ppm was required to induce narcosis in dogs and rabbits over the same exposure period. Cardiac irregularities were observed in electrocardiograms of dogs exposed to 100,000 ppm for less than 4 hours.

In addition, the observation of other side-effects suggested further systemic disturbances associated with acute exposure. Guinea pigs exposed to 5,000 ppm of vinyl chloride for a 30 to 60 minute period displayed pulmonary edema and hyperemia (excess blood) in the kidneys and liver on autopsy.[11] Although all pathological parameters appeared normal in rats exposed to vinyl chloride levels up to 100,000 ppm over a thirteen day period, advanced lymphocytic hyperplasia of the spleen was observed.[12] At lower exposure concentrations and extended exposure periods (50,000 ppm; 19 days), increased liver size was observed in these experimental animals (Sherman rats).[12] Pathological examinations revealed congestion at the cellular level in the liver of these experimental animals; however, parasitic cysts were also observed in the liver of these animals which confounds conclusions regarding acute effects and systemic damage associated specifically with vinyl chloride exposure. Although the results available suggest only marignal systemic effects, there are some indications that vinyl chloride is not simply absorbed and exchanged in the lungs but distributed throughout the body with pathological alterations observed in the liver, kidneys and spleen. Therefore, effects such as pulmonary edema, tracheal irritation, hyperemia of the

liver and kidneys, cardiac arrhythmia and hyperplastic changes in the spleen and liver may be subtle side effects of acute vinyl chloride exposure that suggests functional interaction in various organs and systems of the body. A summary of these and other experiments are presented in Appendix B.

7.1.3 Chronic Inhalation Toxicology

While investigations of short duration with high exposures are useful in determining lethality and gross toxicity, chronic effects associated with continuous or repetitive exposure to lower levels of vinyl chloride are more important in evaluating possible environmental hazards. Several investigations designed to assess chronic effects associated with repetitive exposures to vinyl chloride began in the early sixty's. Torkelson, Oyen and Rowe[13] reported results of studies using several species of animals (dogs, Guinea pigs, rats and rabbits) exposed to levels of vinyl chloride ranging from 50 to 500 ppm. The results of these studies noted that all species of experimental animals exposed to vinyl chloride at 500 ppm administered daily 7 hours/day over a four and a half month period, were normal with respect to appearance, growth and mortality. While several blood parameters (serum enzymes) used to monitor functional disturbances of the liver were found to be within normal limits, there was an increase in liver size observed in male rats that was not apparent in female animals. In addition, central lobular degeneration of the liver and renal tubular damage in the kidneys was apparent upon microscopic examination of the various tissues excised

from animals sacrificed at the end of the experimental period. Since considerable liver damage is required to alter serum enzyme levels used to monitor liver function,[14-16] histopathologic changes such as those observed in these studies may be an important parameter in evaluating beginning liver damage which might not be detected by serum enzymes. Similar effects were observed in the liver of male rabbits exposed to 200 ppm of vinyl chloride administered for 7 hours / daily over a six month period with

necrosis and periportal cellular infiltration in the liver was not observed in the females. This observation suggests a sexual difference in the response of male and female rabbits to vinyl chloride and alludes to a possible hormonal influence. Other experiments suggests that carcinogenic agents may modulate the activity of steroidal hormones.[17-19]

While the liver of male and female rats remained increased in size at this dose level (200 ppm), no apparent microscopic-pathology was observed. There were no apparent kidney disturbances noted among the various animals exposed to this dose level (200 ppm).

Increased liver size was sustained even when exposure was reduced to 100 ppm for 2 hours daily over the 6 month period of the experiment. However, it is important to note that

liver to body weight ratios were not statistically different from controls at these lower dose levels. A further reduction in exposure to 50 ppm for 7 hours per day for 5 days per week administered over a 6 -month period produced no evidence of liver abnormalities in size or microscopic appearance in these experimental animals. Despite the lack of statistical significance,

these toxicologists placed sufficient weight on their observations of subtle liver damage observed in several animal species to recommend adjustments in the established industrial standards for permissible exposure to vinyl chloride as early as 1961.

The experimental protocols used in this investigation were limited to a six month period and did not reserve treated animals for longevity studies. It is conceivable that carcinogenicity of vinyl chloride would have been known nearly fifteen years ago had the effects of longevity been studied in these early studies.

Attempts by Viola et al.[2,20,21] to develop an animal model to investigate the pathogenesis of acroosteolysis revealed convincing evidence of systemic toxic effects in a wide variety of organ systems. These subacute studies provide a more complete description of systemic effects associated with exposure to high concentrations of vinyl chloride monomer extended over a twelve month period. While attention is focused upon the liver of these experimental animals (Rats, Wistar strain) pathology was noted in the kidneys, arteries, skin, bones, brain,and nerves. A fibrosclerotic

reaction appears to be a common denominator in the biologically diverse tissues of these various organs. A fibrotic lesion in the liver appears to be important in evaluating the pre-cancer state of liver angiosarcoma.[22]

These observations provided evidence of the permeation of vinyl chloride throughout the body and suggested interference with membrane structure (e.g. lipid peroxidation) with a compensatory repair response (endothelial proliferation). Carbon tetrachloride also produces a peroxidative degradation of structural lipids particularly in the liver.[23,24]

There have been other published reports in the Russian and European literature that provide evidence of alterations in cardiac function, hypertension, and increased adrenalin and neural activity in the brain of several animal species subjected to low chronic exposure levels of vinyl chloride (Appendix B). These experiments suggest the possibility of cardiac disturbances and behaviorial changes in man exposed to vinyl chloride under occupational circumstances.[25]

A summary of chronic systemic effects from inhalation of vinyl chloride observed in experimental animals include:

- Alteration in liver function. There may be sexual differences in nature of the response of the liver of male and female animals. A fibrosclerotic reaction in necrotic areas of the liver with evidence of a hepatic regenerative process has been noted. Therefore, vinyl chloride may be considered a chemical hepatotoxin.

- Disturbances observed in the circulatory system include irregularities in cardiac function, endothelial fibrosis in arteries and alteration circulating white blood cell levels. Hypertension has also been observed and may be related to induced adrenalin activity similar to other aliphatic chlorohydrocarbons.

- Exposure concentrations, duration of exposure and frequency of exposure appears to be important aspects that determine the nature and severity of toxic response.

The significance of the evidence from chronic studies appear to have been underrated since many of these experiments have not been repeated on a large scale until recent discovery of carcinogenic activity. Although attempts were made to establish a dose-response relationship, there has been little or no data available to permit quantitative analysis of the systemic response to vinyl chloride exposure. Qualitatively, it is important to recognize the significance of repetitive exposures and exposure durations that permit observations of time-dependent response phenomena.[2-5,12,13]

7.1.4 Carcinogenicity of Vinyl Chloride

There have been three investigations that deal with the carcinogenicity of vinyl chloride, Viola et al[2] Maltoni and Lefemine,[4] and Keplinger et al[5] The first evidence of carcinogenic effects associated with exposure to vinyl chloride was reported by Viola et al.[2,21] These investigations involved twenty-five Wistar (AR/IRE) albino male rats (150 gm body weight) exposed to 30,000 ppm of VCM for 4 hours a day, 5 days a week for 12 months. The tumors observed under these subacute exposure conditions are presented in Table 7.1

Although these experiments apparently were not specifically designed for investigating carcinogenicity, there was sufficient evidence of a tumorogenic response to warrant further investigation. Particular attention focused upon the following aspects of tumorogenicity of vinyl chloride in Wistar rats subjected to subacute exposure conditions:

- Tumor multiplicity with neoplastic lesions observed in several tissues.

- The presence of Zymbal gland tumors. These sebaceous glands located in the ear of rodents are particularly responsive to other chemical carcinogens (e.g. acetyl-aminofluorine: AAF, polynuclear aromatic hydrocarbons: PNA such as 9,10-dimethyl-1,2 benzanthracene; urethan; 4 amino-stibenes, benzidine). (4)

Since the majority of tumors observed were epidermoid carcinomas of the skin, these investigators concluded that the cutaneous system (skin) was the system most susceptable to the oncogenic effects of vinyl chloride (Tables 7.1.1 and 7.1.2)

It is important to note, however, the absence of liver angiosarcoma in these animals subjected to high levels of vinyl chloride monomer for nearly half of their life-span.

Therefore, a more comprehensive, quantitative and systematic series of investigations were initiated in Europe and the United States to confirm the carcinogenicity of vinyl chloride with particular emphasis placed upon the dose-response relationships in several studies of experimental animals.

Tables 7.1.1 TYPES OF TUMORS OBSERVED IN MALE WISTAR RATS EXPOSED TO 30,000 ppm OF VINYL CHLORIDE [a]

Wistar Rats number	Tumors		
	Skin	Lungs	Bones
1	Mucoepidermoid carcinoma	Adenoacanthoma	Osteochondroma
2, 3	Epidermoid carcinoma, keratinizing type	No tumor	No tumor
4	Epidermoid carcinoma, keratinizing type	Adenocarcinoma	No tumor
5	Papilloma, keratotic type	No tumor	Osteochondroma
6	Epidermoid carcinoma	No tumor	Osteochondroma
7	Epidermoid carcinoma	No tumor	No tumor
8	Mucoepidermoid carcinoma	No tumor	Osteochondroma
14	Epidermoid carcinoma	No tumor	No tumor
16, 17	Epidermoid carcinoma	Adenocarcinoma	No tumor
21	Epidermoid carcinoma	No tumor	No tumor
22	Epidermoid carcinoma	Adenocarcinoma	Osteochondroma
23	Epidermoid carcinoma	No tumor	No tumor
24	Epidermoid carcinoma	Mucus-producing adenocarcinoma (alveolar cell carcinoma?)	No tumor
25	Epidermoid carcinoma	No tumor	No tumor
26	Epidermoid carcinoma	Squamous cell carcinoma	No tumor

[a] Inhalation exposures were conducted 4 hours/day, 5 days/week over a 12 month period From Viola, P.L. et al.[2]

Table 7.1.2 TUMOR INCIDENCE IN MALE WISTAR RATS EXPOSED TO VINYL CHLORIDE [a]

Vinyl chloride ppm	Total Animals	Tumors			
		Skin	Lung	Bones	Total
30,000	26	17	6	5	25
Controls	25	---	---	---	0

a Inhalation of 30,000 ppm vinyl chloride, 4 hours/day, 5 days/week over 12 months. From Viola, P.L. et al.(2)

In Europe, additional investigations began in late 1971 under the auspecies of Maltoni and Lefemine.[4] A series of 14 correlated and integrated experiments were designed to elucidate the relationship of vinyl chloride carcinogenicity to route of administration, exposure concentration, length of exposure, species response variation and age dependent effects. The basic design of these studies placed particular emphasis upon controlled exposure conditions and a compilation of a tumor incidence profile from observations over the entire life span of the experimental animals in response to inhalation of vinyl chloride of high purity (99.99percent). The preliminary results of this initial study have been reported (Table 7.1.3. The percentage of Sprague-Dawley rats with various types of tumors observed following cessation of vinyl chloride exposure at various dose levels is presented in Figure 7.1.1. The information available from these early studies indicate that vinyl chloride carcinogenicity is dose-dependent. Total tumor incidence appears to decrease with decreasing concentrations of vinyl chloride and was also observed to be dependent upon duration of exposure as well as concentration. Liver angiosarcoma and nephroblastoma of the kidneys of these Sprague-Dawley rats do not appear to be as concentration-dependent as the generalized tumorogenic response (Figure 7.1.1). These investigators suggest that liver angiosarcoma and nephroblastoma may be more dependent upon duration of exposure than upon the concentration of vinyl chloride administered. The basis for this suggestion stems from the observation that

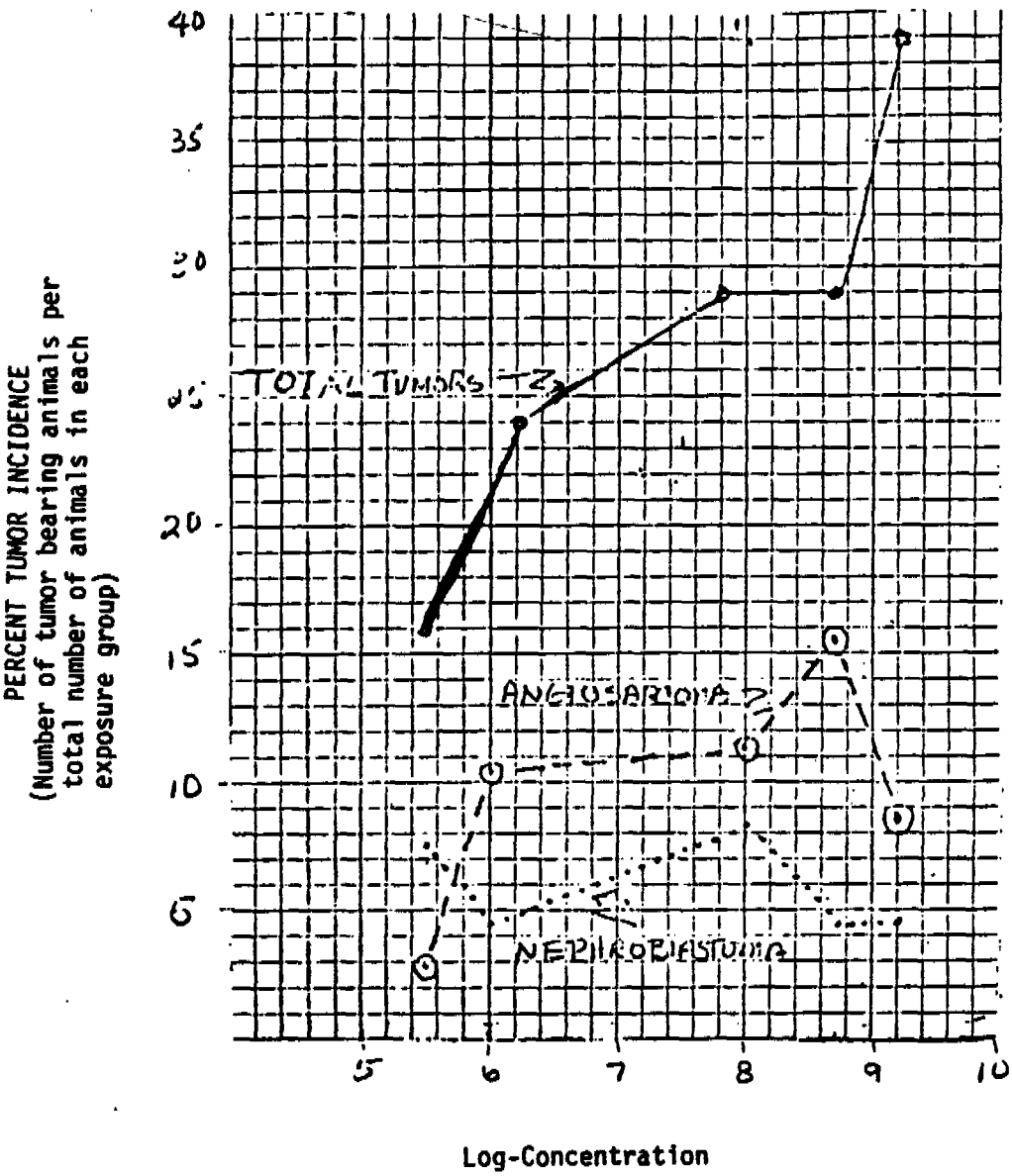
Table 7.1.3 VINYL CHLORIDE CARCINOGENICITY IN SPRAGUE-DAWLEY RATS. PRELIMINARY RESULTS FROM MALTONI AND LEFEMINE[4]

Preliminary Results After 131 Weeks Exposure: 4 hours/day, 5 days/week Over a Twelve-Month Period *

Groups and treatment	Animals (Sprague Dawley rats) Total	Survivors	Animals with tumours: Zymbal glands carcinomas[a] No.	Nephroblastomas[b] No.	Angiosarcomas Liver[c] No.	Angiosarcomas Other sites No.	Other type and/or site No.	Total No.[=]
I VA 2500 ppm	96	-	-	-	-	-	-	-
II VC 10,000 ppm	69	-	13	3	6	-	5[h]	27
III VC 6000 ppm	72	-	5	3	11	1[d]	1[i]	21
IV VC 2500 ppm	74	-	2	6	9	3[e]	1[j]	21
V VC 500 ppm	67		3	3	7	2[f]	1[k]	16
VI VC 250 ppm	67	1		5	2	2[g]	2[l]	11
VII VC 50 ppm	64	3				-		
VIII No treatment	68	1	-		-	-	-	-
Total	577	5	23	20	35	8	10	96

[a] Metastases to lung.
[b] Metastases to liver and or to lung and spleen.
[c] Metastases to lung.
[d] Angiosarcoma in subcutaneous fibrosing angioma.
[e] Two intra-abdominal angiosarcomas (1 contiguous to spleen and 1 to ovary); 1 ossifying angiosarcoma of neck.
[f] One pulmonary angiosarcoma; 1 angiosarcoma of uterus.
[g] One intra-abdominal angiosarcoma (near to spleen); 1 intrathoracic ossifying angiosarcoma.
[h] Two Zymbal gland adenomas; 1 neurilemmoma of the ear; 1 mammary carcinoma; 1 cystoadenocarcinoma of ovary.
[i] Sebaceous gland carcinoma of skin.
[j] Zymbal gland adenoma.
[k] Minimal deviation hepatoma.
[l] One Zymbal gland adenoma; 1 salivary gland carcinoma.
[=] Total No. of tumours.

Figure 7.1.1 The Concentration Dependency of Selected Neoplasia in Sprague-Dawley Rats.[a]



[a] Derived from Maltoni C. and Lefemine, G., 1974.[4] The incidence of neoplasia determined at 131 weeks following the onset of exposure. Animals were exposed to various concentrations of vinyl chloride for 4 hours per day, 5 days per week over a 52 week period. Control animals were void of tumors.

all of the tumors observed under reduced exposure conditions were carcinomas of the Zymbal gland. There were no angiosarcomas or nephroblastoma in the liver and kidneys observed under reduced durations of exposure to high levels of vinyl chloride. However, information is available only at the higher exposure levels of vinyl chloride (10,000 and 6,000 ppm).

There have been five distinct types of tumors observed in the investigations of Maltoni and Lefemine.[4] Angiosarcoma, particularly in the liver of mice and rats were found. This tumor type was also observed in the subcutaneous tissue of offspring from vinyl chloride exposed pregnant rats. Zymbal gland carcinomas and renal nephroblastomas in rats as well as mammary carcinomas in mice as a consequence of metastases from pulmonary adenomas were also observed. It is important to note that Zymbal gland carcinomas, nephroblastomas and liver angiosarcoma were never observed to occur spontaneously in the strain of Sprague-Dawley rats used in these studies.[4]

Selected early conclusions reported by Maltoni and Lefemine from their preliminary studies are as follows; (note that parenthetical material has been added for clarity.):

- "Vinyl chloride is oncogenic (carcinogenic) under the experimental conditions employed. It induces, in rats, carcinomas of the Zymbal glands (sebaceous glands of the skin located in the ear), nephroblastomas (kidneys) and angiosarcomas in the liver and other sites; in mice, liver angiosarcomas, pulmonary adenomas (in the lungs) and mammary carcinomas (breast)."

- "A direct relationship exists between dose (concentration) and length of treatment (exposure duration) and the neoplastic response (carcinogenicity)."

- "Blood vessel ectasis and endothelial hyperplasia, associated or not with cellular atypia, are often observed in the liver and in other organs and tissues in treated animals, with or without angiosarcomas. Therefore, the effect of vinyl chloride on blood vessels and endothelial should be considered systemic."

The American investigation began after the onset of the European studies and were designed to compliment the work of Maltoni and Lefemine.[4,5] While the experimental design differs to some extent from those of Maltoni and Lefemine, the early results from investigations conducted by Keplinger et al.[5] confirm the capacity of vinyl chloride to induce hepatic angiosarcoma in mice at an exposure level of 50 ppm. Angiosarcoma was also identified in the liver of male rats and hamsters exposed to 2500 ppm and one female rat exposed to 200 ppm.[5] Furthermore tumors at other sites of the body were also observed in mice and include those identified in lungs, mammary glands and skin. Therefore, additional evidence of multifocal carcinogenicity of vinyl chloride is consistent with that of Viola et al.[2] and Maltoni and Lefemine.[4] It is important to note the appearance of liver angiosarcoma in a third species of experimental animals exposed to gaseous vinyl chloride; the Golden Syrian hamster. There have been no tumors observed in control animals at this time. Although there has been a high mortality rate among experimental animals in these studies, it is important to note

that angiosarcoma of the liver has been observed in mice exposed to 50 ppm of vinyl chloride following periods of exposure of only 6 months duration. This tends to confirm the observations of Maltoni and Lefemine in rats at this exposure level, and helps to clarify some questions raised regarding whether liver angiosarcoma occurs within the life span of experimental animals. In the Maltoni experiments, liver angiosarcoma was observed at 50 ppm only after 130 weeks of observation, suggesting that at dosages below 50 ppm, effects might not occur within the lifetime of rats. The American studies would suggest that,at least in mice, this is not so.

The preliminary results from the American and European investigations provide convincing evidence that vinyl chloride is an active chemical carcinogen. It has been shown to induce tumors in various organs in three species of animals at exposure concentrations down to 50 ppm. Angiosarcoma has also been observed in three species of animals; Sprague-Dawley rats, Syrian golden hamsters and mice. Angiosarcoma of the liver has also been observed in rats and mice in two research laboratories at 50 ppm exposure concentrations. It is noteworthy that Wistar strain rats display a multiple carcinogenic response following inhalation of vinyl chloride with tumors appearing in several different organs (bone, kidneys and skin), but this strain of rats is apparently refractory in the development of liver angiosarcoma.[2,5] Furthermore, recent evidence suggests that the oncogenic response in the liver of experimental animals is not restricted to angiosarcoma since hepatomas have also been observed as well.[26]

While two laboratories[4,5] are investigating the dose-response relationships of vinyl chloride carcinogenicity, only the studies of Maltoni and Lefemine are sufficiently advanced to provide information in this regard. However, the published data available are preliminary, largely qualitative in nature and of limited value for statistical analysis and risk assessments (Appendix A). Specific attention is drawn to the presentation of tumor incidence and the absence of data regarding the precise number of animals bearing more than one tumor type (Table 7.3). Although total tumor incidence appears to be more dependent upon exposure concentration, this dependency is not readily apparent regarding liver angiosarcoma and is absent regarding nephroblastoma of the kidneys (Figure 7.1). Liver angiosarcoma and nephroblastoma appear to be more dependent upon exposure duration than exposure concentration.[4] It is important to recall the preliminary nature of the data available and the nature of carcinogenicity. Cancer is self replicating and largely irreversible depending upon the type and size of tumor development. Liver angiosarcoma in man is largely an incurable, fatal disease. Therefore, exposure to vinyl chloride at any concentration for any period of time may not be without risk.

Another important consideration from the early results of Maltoni and Lefemine is the possibility of transplacental carcinogenicity. Further attention is also drawn to the recent evidence of vinyl chloride mutagenicity that requires biotransformation (metabolic activation) by liver detoxification enzymes before effects are observed

in bacterial test systems.[27]

While somatic mutations may provide a basis for carcinogenicity in the immediate generation, dominant germinal mutations could be expressed as an increase in spontaneous abortions. In this regard, preliminary evidence suggests an elevated incidence of spontaneous abortions among the families of polyvinyl chloride workers. These considerations underline the need to further evaluate the effects of vinyl chloride upon reproductive compentency including fertility, fecundity, and pre-peri-natal toxicology and transplacental carcinogenicity, including possible transmission of this hazardous material from the workplace to the home.

7.1.5 Absorption, Distribution, Metabolism, and Excretion

In the review of aliphatic chlorinated hydrocarbons by von Oettingen,[11] levels of vinyl chloride were determined in the blood of cats subjected to acute exposure conditions. (See Appendix B also). Exposure to 100,000 ppm for less than 4 hours produced vinyl chloride concentrations of 15 to 17 mg percent (mg/100 mg blood) in these animals. Respiratory and cardiac arrest were observed as blood levels of vinyl chloride reached 27 to 30 mg percent and exceeded 40 mg percent respectively. Approximately, 82 percent of the nhaled VC was eliminated immediately from the lungs in these experiments. The observation of Viola et. al.[20] in Wistar rats exposed to 10,000 ppm for 60 minutes tends to support conclusions regarding the lungs as the principle excretory route of vinyl chloride. The concentration of vinyl chloride decreases rapidly in expired air, blood, urine, brain, liver and kidneys during the first hour followiing exposure in those experiments. There was essentially no detectable levels of vinyl chloride in these animals at 3 hours following exposure. Analysis of the distribution of vinyl chloride among the formed elements and the fluid media of the blood indicates that red blood cells appeared to have a greater affinity for vinyl chloride than serum. Although these observations are limited in scope and detail, they provide qualitative evidence that vinyl chloride is absorbed, distributed throughout the body,and eliminated by the pulmonary and urinary excretory routes. It would appear from these early studies that vinyl chloride was not metabolized,was excreted essentially unchanged and tended to support conclusions regarding its low order of toxicity.

However, with the evidence of the more recent studies on carcinogenicity, investigations regarding the metabolism and pharmacodynamics of vinyl chloride under controlled conditions have been undertaken by Hefner et al.[29,30] Preliminary results of this investigation indicate that vinyl chloride monomer apparently metabolized to polar metabolites that are excreted primarily in the urine of animals subjected to an initial 50 ppm exposure level. There appears to be very little excreted in the expired air as unaltered vinyl chloride at this exposure concentration.

The early conclusions drawn from these investigations by Hefner et al. are as follows:

- There appears to be a metabolic threshold for metabolism of vinyl chloride. Spraque-Dawley rats exposed to vinyl chloride below 100 ppm appear to metabolize vinyl chloride fairly readily. Exposure to vinyl chloride levels in excess of 200 ppm reduces metabolism considerably. This also suggests that the metabolic pathway available at levels of vinyl chloride below 100 ppm can be saturated.

- Vinyl chloride appears to be metabolized via alcohol dehydrogenase since it can be inhibited by pyrazole (1,2 pyrazole and ethanol. It is important to note that the metabolism of vinyl chloride did not appear to be inhibited by SkF-525-A that is used to block the activity of some microsomal enzymes. Microsomal enzymes are important in steroid metabolism and detoxification of foreign chemical compounds (xenobiotics). While these are preliminary conclusions, it is important to recall the appearance of hepatic angiosarcoma in two species of experimental animals at 50 ppm exposure level (rats, mice) which would argue against a metabolic carcinogenic threshold at 50 ppm and higher exposure levels.

- The evidence presented in these studies suggests alternative metabolic pathways for vinyl chloride resulting in metabolites of perhaps differing toxicity. However, the saturation of the presumably safer pathway by ethenol,(and,conceivably by other substances as well. i.e. drugs) argues that the "distinction" between pathways may not be well defined and that under certain conditions even relatively low exposures might be shunted through the more toxic pathway. Furthermore due to genetic variability, some individuals may

metabolize vinyl chloride predominantly through the more toxic pathways. In this regard, it would be premature to conclude, based upon current evidence, that an acceptable exposure to vinyl chloride can be defined in terms of alternative metabolic pathways.

Vinyl chloride has been found to be excreted as S-hydroxycysteine, suggesting metabolic transformation via an expoxide intermediate. The elimination of xenobiotics by the formation of epoxide, followed by conjugation with thiol containing compounds is found in the metabolism of a number of carcinogenic compounds, as will be discussed below.
Since vinyl chloride has is a rather simple chemical structure with limited capacity for metabolism by complex pathways, it appears to be a good model compound for use in studies on the mechanism of chemical carcinogenesis.

P. L. Grover, P. Sims and their co-workers have tested a number of carcinogens for <u>in vivo</u> and <u>in vitro</u> formation of epoxides, which have been shown to be alkylating agents of nucleic acids and proteins.[3,29-33]
They have presented evidence for formation of epoxides for a number of carcinogens including pyrene,[34] benzo[a]pyrene[34] phenanthrene,[35] benz[a]anthracene[35] and dibenz[a,h]anthracene.[35] Epoxides of polycyclic hydrocarbons have been shown to be mutagenic to T_2 bacteriophage, to bacteria,[37] to <u>Drosophila sp.</u>[38] and to mammalian cells.[39]
They also produce malignant transformations of cells in culture.[40]

Another possible mechanism of cancer induction by chemicals is via decreased protection against the deleterious effects of free radicals. Non-protein thiols are known to afford protection against free radicals. However, these thiol containing compounds can be reduced by the formation of mercapturic acid conjugates of epoxides from reaction with glutathione.

Hefner et.al.[29] also reported a decrease in serum non-protein thiol compounds after exposure of rats to vinyl chloride. This can be related to the dangers of multiple exposure to compounds related to vinyl chloride in the same manner as for the epoxide mechanism. Indeed, this mechanism is only a variation of the epoxide mechanism, however, in this case free radicals are the final cause of damage, whereas in the epoxide mechanism, reaction of epoxide with DNA or protein is the deleterious step. A large literature also deals with the formation of mercapturic acid derivatives of epoxides from reactions with glutathione. A review of postulated mechanisms of carcinogenicity of vinyl chloride and structurally related compounds has been presented by van Duuren.[8]

It would be ideal to suppose that a screening procedure for carcinogenic chemicals could be developed on the basis of analysis of tissue from experimentally exposed animals for epoxides or mercapturic acid derivatives. The concentration of these materials found at various exposure levels could theoretically be used as a risk index. However, discrepancies in the relationship of these derivatives to carcinogenesis preclude any such simplistic approach. The data herein alluded too does, however, indicate that such an approach may be possible in the future if research pertinent to the basic mechanisms of chemical carcinogenesis is supported.[41,42] This research should optimistically result in answers that would allow evaluation of the carcinogenic hazard of a large number of existing environmental pollutants as well as analysis of new synthetic chemical compounds prior to their ubiquitous distribution in the environment.

7.1.6 Additional Toxicological Concerns

7.1.6.1 Toxicity of Polyvinyl Chloride

The free radical content and the level of residual vinyl chloride monomer of PVC resins and plastic end products could affect their toxicity including potential for carcinogenic activity. Volkeimer[43] reported particles of polyvinyl chloride up to 70 microns in diameter transported and deposited throughout the tissues of experimental animals. The combination of these two observations along with the possibility for population exposure to polyvinyl chloride such as perhaps through erosion of PVC pipe and the wide use of flexible plastic materials containing leachable materials indicate the necessity for further study in this area.

7.1.6.2 Toxicity of Pyrolytic Products of PVC

Another potential problem area related to vinyl chloride is the composition and toxicity of products produced by incineration of PVC. Again this is a potentially widespread opportunity for general population exposure to other hazardous materials. Disposal of PVC by incineration is a common practice, however, little data is available on the toxicology of pyrolytic products.

7.2 THRESHOLD LIMIT VALUES

Although occupational health studies began in 1930, there were essentially no reports of possible systemic effects or serious health adversities associated with polyvinyl chloride production and/or exposure to vinyl chloride monomer (VCM) until 1949. Chronic "epithelial" hepatitis was diagnosed in Russian resin fabricators engaged in processing polyvinyl chloride resins.[9] The possible etiological agents listed included primary ingredients used for polymerization, compounds released from the resin during processing and plastisizers. It is noteworthy that the possibility of potential health hazards from exposure to residual materials released from polymer resins was suggested more than twenty five years ago. In the absence of chronic investigations during this period, the low acute toxicity and the apparent lack of evidence of adverse health effects from previous occupational experience,a threshold limit value of 500 ppm (1300 mg/m^3) time-weighted average was established in 1959 by the American conference of Governmental and Industrial Hygienists (ACGIH) as the industrial hygiene standard for vinyl chloride in the United States. The non governmental standard was apparently based solely upon fire and explosive hazards that are possible at a minimal level of 2.5 percent (25,000 ppm) by weight of vinyl chloride in air.

The results of acute toxicity studies, which were the order of the day in the early years of vinyl chloride and polyvinyl chloride production, provided evidence of pulmonary congestion (edema) with damage noted in the liver, kidneys and tracheal epithelium concomitent with narcotic effects associated with high exposure levels of short duration. Advancements in toxicological protocols and the state-of-the-art of biomedical research along with the evidence of organ damage and systeric effects observed under acute exposure conditions led to the chronic (low level) inhalation studies of Torkelson, Oyen and Rowe in 1961.[13] Based on observations in several species of experimental animals that included evidence of liver and kidney pathology at the threshold limit value (500 ppm) and the absence of these effects at 50 ppm following 6 months of investigation, these authors recommended a change in the industrial hygiene standard. Those recommendations made in 1961 suggested limiting occupational vinyl chloride exposures to less than 100 ppm with a time-weighted average not to exceed 50 ppm in air of the PVC workroom environment.

The subacute studies of Lester, Greenberg and Adams[12] led the authors to conclusions that were essentially contradictory to those of Torkelson, Oyen and Rowe, despite increased liver weight and slight liver histopathology observed in their experimental animals. On the basis of these and other observations at higher dosages administered over shorter exposure periods, these authors recommended maintaining the existing 500 ppm threshold limit value.

The Committee on the Threshold Limit Values of the American Conference of Governmental and Industrial Hygienists (ACGIH) considered the evidence presented in these two conflicting reports and chose to change the industrial hygiene standard for vinyl chloride from a 500 ppm maximum time-weighted average (TWA) value to a 500 ppm ceiling level for industrial exposure.

Along with growth and expansion in production and use of polyvinyl chloride resins, the workforce in this industry increased accordingly. In time a unique occupational health problem appeared involving those workers engaged in cleaning polymer reactor vessels. Vinyl chloride disease or acroosteolysis was first reported in 1966.[9] This disease involved a progressive skeletal deterioration of the fingers accompanied by interference in peripheral nerve response and diminished blood circulation (Raynaud - like syndrome). While other reports have appeared in subsequent years, occupational acroosteolysis in PVC reactor cleaners has been well documented by large scale epidemiological studies conducted between 1969 and 1972.[1,9] Since this adversity was apparently restricted to those individuals exposed to exceptionally high levels of gaseous vinyl chloride and the response associated more with direct dermal contact with PVC resins, it appeared that the processing of PVC resins did not involve a health hazard of sufficient severity to warrant adjustment of the industrial hygiene standard. Furthermore, available standard textbooks and review articles have stressed the safety of polymer processing and noted only a minimal risk of narcosis associated with inhalation of vinyl chloride vapors.[47-50]

Important studies regarding occupational exposure to vinyl chloride that were influential in adjusting permissible exposure levels were those of Baretta, Steward and Mutchler[46] and Kramer and Mutchler.[44] These investigations involved determining levels of vinyl chloride in the air of the work area and correlating them with results of a systematic multiphasic screening of employees using a variety of clinical parameters. The mean concentration of vinyl chloride in the work-place air in these studies was found to be 160 ppm with a range of 30 to 170 ppm. Vinylidine chloride was noted as a co-contaminant at a level of 5 ppm. While no difference was observed in blood pressure, hemoglobin levels, electrocardiograms nor was there evidence of morphological anomalies (acroosteolysis), there was adequate indication of some degree of liver damage among PVC employees at TWA exposures of 300 ppm. These observations led the investigator to conclude that there was a definite risk of liver damage at vinyl chloride levels of 300 ppm time-weighted average (in the presence of 5 ppm of vinylidine chloride).[44]

The second adjustment of the industrial hygiene standard to a TWA of 200 ppm was apparently influenced by evidence of human liver dysfunction and the availability of monitoring data regarding levels of vinyl chloride in air of at least one PVC production facility. [44,46] Although Torkelson et al. had reported slight liver damage in experimental animals exposed to 200 ppm of vinyl chloride in 1961, [13] these observations were apparently not fully considered until a decade later.

Due to the increasing incidence and concern regarding acroosteolysis, experimental studies had been undertaken to develop an animal model for elucidating the pathogenesis of this and other adverse effects observed in humans exposed to high levels of vinyl chloride by Viola et al. in 1970 and 1971. [2,20,21] In the course of these acute studies carcinogenic effects were observed and

presented in 1970 with a later full detailed publication of the observations in 1971.

Although deficiencies in experimental design were noted with regard to those suitable for carcinogenic investigations, there was sufficient evidence presented that warranted further study. Subsequent investigations were initiated in Europe and in the United States using lower exposure levels and purer compounds.[4,5] Preliminary results from these efforts confirmed the carcinogenicity of vinyl chloride in several species of experimental animals, a dose-response dependency of tumor incidence was observed, and positive effects detected at exposure levels down to 250 ppm.[3,4]

While carcinogenic effects of vinyl chloride were noted at dosages close to permissible industrial exposure levels (TLV: 200 ppm), there was equal concern regarding the type of tumors identified and not observed at higher exposure levels in the earlier studies of Viola et al.[2] in Due Due to the history of liver dysfunction in PVC employees and in chronic experimental animals observed earlier particular concern was aroused by the appearance of liver angiosarcoma in experimental animals.[3,4]

Increasing interest in vinyl chloride followed the findings that 4 employees at this a PVC plant had died of either liver angiosarcoma, a rare form of human liver cancer, or other liver cancers of unknown types from 1968 to 1973.[6] A fifth individual died in late 1973 of cirrhosis of

the liver. Investigation of the exposure history of these individuals revealed that the deceased employees had an average exposure of 19 years to vinyl chloride and ten years to vinylidene chloride. These workers had been engaged in operations where vinyl chloride concentrations may have greatly exceeded the 1972 Threshold Limit Value (200 ppm).

In view of these considerations and results from on-going toxicological studies, government officials pursuant to the statuatory requirements of the occupational safety and health legislation of 1970 promulgated an emergency standard for

industrial exposure at 50 ppm in early 1974 as efforts to determine the scope of the occupational problem were accelerated.[51] Results of the American and European toxicology studies soon revealed the induction of liver angiosarcoma and other tumors at a 50 ppm exposure level of vinyl chloride.[3-5] Industrial epidemiological investigations identified additional cases of liver angiosarcoma among American and European PVC workers. An occupational standard of 1.0 ppm (or detectable levels) was then proposed by the Occupational Safety and Health Agency, U. S. Department of Labor as an industrial exposure standard for vinyl chloride in American industrial facilities.[52] Subsequently, a permanent 1 ppm time-weighted average occupational standard (8 hours per day; 5 days per week) with a peak 5 minute excursion not to exceed 5 ppm has been promulgated.

Angiosarcoma of the liver is an extremely rare tumor in the general population of the United States. The incidence of angiosarcoma among employees involved in the manufacture of monomeric vinyl chloride and polyvinyl chloride resins substantially exceeds the estimated national incidence level. During the course of retrospective analysis of various tumor registries, several community cases of liver angiosarcoma were discovered. Although the general public has been exposed

to vinyl chloride thorugh other exposure routes (e.g. aerosol sprays), particular concern has been expressed regarding community cases of liver angiosarcoma among those with residence situated near VC/PVC production plants and resin fabricating facilities. Questions have been raised regarding exposure of the more than 700,000 workers employed in fabricating PVC resins containing residual monomeric vinyl chloride as well as the degree of community exposure surrounding these plants. It is noteworthy that the first reported occupational health problems associated with polymer processing involved workers engaged in fabricating resins into plastic products. (a) Vinyl chloride has been detected in the ambient air near vinyl chloride and polyvinyl chloride production sites.

The appearance of liver angiosarcoma in experimental animals serves to underscore the predictive value of well designed and executed toxicological studies in identifying potential health hazards to man. While it is always a curiosity to ponder speculations on a retrospective basis, had adequate studies been performed at an earlier date, the problems associated with vinyl chloride exposure may well have been identified before human cases of liver angiosarcoma among PVC workers had occurred.

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7.3 HUMAN EFFECTS

To date most of our knowledge of undesirable effects associated with vinyl chloride exposure in man comes from occupational situations. These effects include an increased risk of cancer at multiple organ sites including angiosarcoma of the liver, an almost invariably fatal form of liver cancer. Liver angiosarcoma is extremely rare among the general population but has been observed among workers with exposure to vinyl chloride. It is recognized that

angiosarcoma observed today in workers exposed to vinyl chloride was generally, though not exclusively, the result of very high occupational exposures received many yeara ago. The latent period for angiosarcoma of the liver has been estimated at between 15-20 years following onset of exposure although individual cases may occur after shorter or longer latent periods.[1,2]

This long latent period suggests that the full impact from past vinyl chloride exposure among workers may not be realized until many years from now since the greatest number of workers have had onset of exposure in the last decade. For example, of the 25 known occupationally reported cases of live angiosarcoma, information as to date of diagnosis or death, where available, indicates that only 2 of 22 cases died prior to 1965 and that 14 of 22 cases had died or were diagnosed in 1970 or later.[2] Accordingly estimates of cancer risk from vinyl chloride based upon data available today may well understate the magnitude of this problem. In this regard, increased awareness and improved diagnostic procedures may in part also contribute to future increases in reported cases of liver angiosarcoma.

To date surveys have uncovered 15 cases of occupationally reported liver angiosarcoma in this country.[2] Of these cases. 14 have been among workers in PVC polymerization plants and one case involved an accountant employed at

a vinyl cloth plant. At least 13 of these cases have been comfirmed as angiosarcoma of the liver by pathologists at the National Cancer Institute.[3] In addition to these 15 U.S. cases, 10 occupational cases of liver angiosarcoma have been reported from European countries, 7 among workers in the PVC polymerization industry and 3 among non-polymerization workers. A summary of these reported occupational liver angiosarcoma cases is shown in Tables 7.3.1 and 7.3.2.

As indicated in these tables, the latent period from onset of initial exposure to age at diagnosis or death in all known instances is 10 years or greater. Similarly the years of exposure among these individuals preceding development of clinical disease is with one exception also in excess of 10 years. This one exception may, however, be important and involves a case in which there was an established occupational exposure history of only 4 years' duration. This case suggests that disease may, in certain instances, develop after relatively brief durations of occupational exposure to vinyl chloride or, alternatively, that other factors besides vinyl chloride may have been involved. These cases represent all currently known occupationally reported liver angiosarcomas. A reported case of liver angiosarcoma in an employee at an electrical insulation plant in Connecticut upon re-examination by pathologists at the National Cancer Institute, was not considered to be liver angiosarcoma.[4,5,6]

With respect to the general population, at one time there were believed to be 3 reported cases of liver angiosarcoma among individuals who had resided in the vicinity of industrial vinyl chloride emission sources. A review of these cases by pathologists at the National Cancer Institute has confirmed the diagnosis of liver angiosarcoma in two of the three instances. One

Table 7.3.1

LIVER ANGIOSARCOMA CASES AMONG
VC POLYMERIZATION WORKERS[2]

Case No.	Country	Date of Death	Years after First Exposure	Years of Exposure	Age at Diagnosis
1	West Germany	1969	11	11	39
2	United States	Alive	12	12	45
3	United States	1971	14	13	37
4	West Germany	1971	14	14	40
5	United States	1968	15	15	44
6	United States	1961	15	15	41
7	United States	1968	17	17	54
8	United States	1969	18	4	41
9	Sweden	1970	19	18	43
10	United States	1969	20	15	50
11	United States	1964	20	18	52
12	United States	1973	22	16	51
13	Norway	1972	22	21	56
14	United States	1970	23	23	60
15	United States	1968	24	18	45
16	United Kingdom	1972	26	20	71
17	United States	1973	28	28	59
18	United States	Alive	29	17	43
19	United States	1974	30	30	52
20	Czechoslovakia		Awaiting Details		
21	Czechoslovakia		Awaiting Details		

Table 7.3.2

LIVER ANGIOSARCOMA CASES AMONG
NON-VC POLYMERIZATION WORKERS[2]

Country	Date of Death	Years after First Exposure	Years of Exposure	Age at Diagnosis	Notes
United States	1973	---	---	47	Accountant at vinyl cloth plant
West Germany	---	14	---	43	Filled pesticide cans with VC propellant
United Kingdom	1970	24	11	55	Vinyl cloth plant
Sweden	1972	27	23	61	VC monomer production plant

case of a woman in Buffalo, New York that was originally believed to be liver angiosarcoma[7] has now been rediagnosed as an anaplastic carcinoma rather than a sarcoma.[8] The two other cases, both from Connecticut, represent confirmed angiosarcomas[6,8,9] but these cases are not identical in all respects to the pathology which has been observed among PVC polymerization workers.[3,9,10] The implications of these dissimilarities between community and occupational cases are not fully understood. Angiosarcomas of the liver resulting at lower exposure doses may not be characterized by all the pathologic findings seen in the PVC workers who in general were exposed to high doses of vinyl chloride. On the other hand, the possibility must also be considered that these two Connecticut community cases were unrelated to vinyl chloride exposures. The fact that Connecticut has one of the finest tumor registries in this country may be important since other states with less adequate followup procedures would not be able to readily identify suspect community cases of liver angiosarcoma. Further the clustering of these 2 community cases and the above mentioned accountant around VCM emission sources in Connecticut raises the possibility of a causal relationship.

Of these community cases, one was a 73-year old man who had lived his entire life within 2 miles of an electrical products factory which processed electrical insulation made of PVC. The other was an 83-year old woman, a housewife and retired cook, who resided for 35 years within ½ mile of the vinyl products plant at which the above-mentioned accountant was employed.[4]

It should also be noted that both community cases lived in excess of 70 years. In contrast, over half of the 25 reported occupational cases mostly at high levels of exposure were either diagnosed or had died at ages 50 years or younger and only one case lived in excess of 70 years. These community cases may reflect an increase in latent period at low levels of exposure as has been suggested in animals studies.[9]

As a result of the reported cases of liver angiosarcoma among vinyl chloride workers, a number of studies have been conducted examining the mortality experience of these workers and contrasting this experience with that observed in the general population.

Tabershaw/Cooper Associates conducted a mortality study of workers in the vinyl chloride industry.[10,11] The objectives of this study were threefold: (1) To contrast the mortality experience of individuals employed in vinyl chloride plants with that of the general population; (2) To examine mortality patterns among vinyl chloride workers in relation to estimated occupational exposure; and (3) To compare mortality patterns among vinyl chloride workers with those for other occupational groups.

The study population was composed of 8,384 individuals from 33 domestic plants with at least one year of occupational exposure to vinyl chloride, including retired and terminated as well as currently employed workers. The vital status of these workers was ascertained as of December 31, 1972 and cause of death was determined based upon available death certificates. Observed mortality was then compared to expected mortality based upon the United States male population accounting for age and time of death and Standardized Mortality Ratios were computed for total mortality and specific causes of death.

Exposure categories were defined subjectively by industrial hygiene and safety personnel at each plant who identified those jobs and work locations with the highest exposures to vinyl chloride and classified other job categories as medium or low relative to those jobs with the greatest exposures. This procedure was reasonable for estimating relative exposure within a given plant but could not assure comparable exposure categories across all plants or over time since a low exposure in past years might be numerically equivalent to a relatively high exposure in recent years. An exposure index was calculated for each worker as a time weighted average

of exposure categories over the period of employment allowing an overall low and a high exposure category to be defined.

Followup procedures were adequate to define the vital status for 85% of the study population as of December 31, 1972. Among the 352 workers known to have died, death certificates were obtained for 328 workers. The mortality calculations considered only those workers who had been successfully traced which assumes that the mortality experience of these workers was equivalent to those who were not successfully traced. The median birth year for those successfully traced was 1931 compared to 1920 for those not traced. The median year in which exposure began was 1962 among those successfully traced compared to 1953 among those not traced. The median duration of employment for those successfully followed was 80 months in contrast to 44 months for those who were not traced. Thus, while those successfully traced had about twice the duration of employment as those not traced, those who were not traced began their employment about 10 years prior to those for whom followup was complete. Accordingly, the mortality experience among those not traced might have been different from that in the study population considering the increased latent period since onset of exposure in this group. More than half (about 60%) of the study population entered employment in 1960 or later indicating that the majority of workers in this study were not followed for an adequate length of time after exposure began to assure observation of all potential long term effects. Included among the 7,128 workers successfully traced, however, were 854 workers with 20 or more years' exposure and 1,640 workers with exposures of 15 years or greater. The discovery of 1,500 workers with exposures

occurring up to 35 years ago -- too late to be included in the study group-- should also be noted since these workers would have provided information as to the effect of very long exposure and long latency upon mortality, areas in which the present study was relatively weak.

The effects of exposure index (low vs high) and duration of exposure (less than or greater than 5 years) upon mortality as well as interaction effects between level and duration of exposure were examined.

Based upon these calculations, the following observations were made:

-- Compared to the general male U.S. population the overall mortality of the study population was approximately 75% of what would have been expected. This favorable overall mortality frequently occurs in occupational groups even if an industrial hazard increases the risk of death from a particular cause, since occupatonal groups are usually younger, and healthier than the average general population.

-- No specific cause of death was increased to a statistically significant extent above what would have been expected in a comparable U.S. male population.

-- SMR's (Standardized Mortality Ratios) for malignant neoplasms as a whole increased with increasing exposure, measured by level, duration or both. For example, 36 malignancies were observed in the high exposure group with 5 years or more exposure compared to 26.11 expected cases. Among those with greatest exposure, cancers of the liver (primarily angiosarcoma), respiratory

system, brain, cancers of unknown primary site and lymphosarcoma occurred more frequently than expected. Though these findings were not statistically significant, the authors of the Tabershaw-Cooper study considered these findings suggestive of a relationship between exposure to vinyl chloride and increased cancer risk at multiple sites, since the number of deaths for many cancer causes in this study is quite small. Accordingly, even relatively high SMR's may not be statistically significant.

The results of a long-term mortality study of 594 chemical workers exposed to vinyl chloride between the years 1942-1960 at the Dow Chemical Company were reported.[12] The study population was defined as production workers at one manufacturing facility who worked in areas with potential vinyl chloride exposure. Each job classification was assigned an exposure rating of low, intermediate, or high depending upon the existing industrial hygiene data. This is the only available mortality study in which vinyl chloride exposures could be reconstructed using actual air measurements. Three categories of exposure were defined based upon estimated time-weighted average concentrations for an 8-hour day. The low-exposure group consisted of those with TWA concentrations below 25 ppm vinyl chloride, the intermediate group had TWA exposures ranging from 25-200 ppm, and the high group was characterized by TWA exposures of 200-300+ ppm. Also included in the high group were those with TWA exposures in the intermediate range but who were also exposed to frequent unpredictable excursions above 1,000 ppm. A fourth category of indeterminate exposure was defined for individuals working in areas where insufficient air monitoring data were available. A subjective evaluation suggested that for these individuals, exposures were mostly in the low to intermediate range.

Assignment to exposure groups was determined by the highest exposure experienced for one or more months. By this procedure, the lowest exposure category contained only individuals with low exposure whereas the highest exposure group included some individuals with predominantly lower exposures. Duration of exposure was considered based upon two categories--less than one year, and one year or longer. Accordingly, effects of longer durations of exposure well above one year were not adequately examined, although the impact of latent period since onset of exposure was considered in the analysis. A number of members in this study (72) had histories of exposure to both vinyl chloride and arsenicals. In view of the cancer risk associated with arsenicals, the employees with arsenic exposure were excluded from dose-response relationships related to vinyl chloride.

Expected deaths in this cohort were determined from United States white male mortality rates. Death certificates were obtained for 86 of the 88 individuals known to have deceased. Of the 148 individuals who had left the company, 131 individuals were successfully traced. Among the individuals who had worked with arsenicals and vinyl chloride, 7 of 10 deaths were due to neoplasms compared to 1.9 cancer deaths expected. No lung cancer was noted in this group. Among workers exposed to VCM but not arsenicals, observed deaths were 91% of the expected deaths based upon the U.S. white male population, suggesting a possible increase compared to other chemical production workers at the same site who experience mortality rates 15-20% below the U.S. white male population. No deaths due to angiosarcoma of the liver or other liver cancers were noted in the group exposed to vinyl chloride

but not arsenicals. For this group as a whole, total malignancies were less than expected; 13 observed compared to 15.4 expected.

The effect of exposure grouping upon malignancy rate was examined for this cohort exclusive of arsenical workers. Of 163 individuals in the high exposure group, only 27 had 20 or more years at low to high exposure and only 19 had 10 or more years of only high exposure. Of the 13 malignancies observed in this cohort, 9 occurred in the high-exposure group, compared to 5.1 expected. Due to the small number of deaths involved, this difference was not tested for statistical significance. To examine for possible latent effects, the mortality experience of workers with 15 or more years since onset of exposure was studied. In this group, 9 malignancies were observed, 8 of which occurred in the high-exposure group. Accordingly, 8 of the 9 malignancies observed in the high-exposure group occurred 15 or more years after onset of exposure. Shown in Table 7.3.3 are summaries of the results.

Based upon this study, the authors concluded that workers exposed to vinyl chloride at levels above 200 ppm experience an "apparent increase in overall malignancy rate." When exposures were kept below 200 ppm a decrease in the malignancy rate was found. Angiosarcomas of the liver were not found at any level of exposure. Among the workers exposed above 200 ppm TWA, the increase in overall malignancy was not statistically significant. The authors also commented as to possible cocarcinogenic effects of other exposures with vinyl chloride, particularly benzene, cigarette smoking and arsenic.

Table 7.3.3

SUMMARY OF DOW MORTALITY STUDY[12]

Study Population
- a) Years exposed: 1 year or more
- b) Onset since first exposure: No restriction
- c) Size of cohort: 594, total;522 with VC exposure only
- d) Number successfully followed up: 577

SMR's (excluding arsenic workers)	O/E	SMR*
All causes	78/85.7	91
All cancers		
a) All VC exposed	13/15.4	84
b) Only high exposure group	9/5.1	176
-- Less than one year exposure	3/2.2	136
--One year or more exposure	6/2.9	209
c) High exposure group with 15 years after onset of exposure	8/3.2	250
-- Less than one year exposure	3/1.3	231
-- One year or more exposure	5/1.9	263

*SMR = standardized Mortality Ratio.

In reviewing these data, certain strengths in this study are evident, expecially the availability of measured vinyl chloride exposures and the successful followup of over 95% of the cohort. Several weaknesses must, however, also be mentioned. The high exposure group was composed predominantly of individuals with a range of exposure from low to high levels. Since only one month of high exposure was required to place an individual in this group only 19 of 163 members in this group, had exposures exclusively to high levels for periods of 10 years or more. Accordingly, though all members in this group experienced some vinyl chloride exposures in the range of 200-300+ ppm TWA, it is likely that this group as a whole had TWA exposures which were, in fact, below 200 ppm when averaged over the work histories of all members in this group. Further, the frequency of high exposure in this group is also not known and this may be important with respect to repair mechanisms. On this basis, increased malignancies might have occurred among individuals with lifetime average exposures below 200 ppm. Another weakness is that duration of exposure to vinyl chloride was not adequately considered in this analysis. For example, 7 of the 9 individuals in the high exposure group with malignancies had been exposed to vinyl chloride for more than 10 years, but only 66 of 163 individuals in the high exposure group had 10 years or more exposure to vinyl chloride. In this regard, reanalysis of the data for those with only 10 years or more exposure might have resulted in greater increases in observed compared to expected malignancy rates.

Monson et. al. conducted a proportional mortality study among workers in a vinyl chloride monomer plant in Calvert City, Kentucky and among workers in a vinyl chloride polymerization plant in Louisville, Kentucky.[13,14] Death certificates were used as a source of cause of deaths and certificates

were obtained for 142/161 white males employed at these plants who were known to have died. When death certificates were not available, cause of death as recorded in company abstracts were used.

Causes of deaths for these 161 individuals were tabulated covering the period 1947 through 1973 and these were compared with the expected distribution of deaths as calculated from proportional mortality ratios for United States white males accounting for age and time of death.

Since mortality patterns among workers in both plants were similar, these groups were combined for purposes of data analysis. Overall, a statistically significant 50% excess in deaths due to cancer was observed. Five cases of liver angiosarcoma were identified in this study in addition to cancers (one each) of the gall bladder, common bile duct and an unspecified case of liver cancer. All told, a 900% excess in cancers of the liver and bilary tract was observed. If the cases of angiosarcoma were excluded from this analysis, a 275% excess in these cancers was observed. Five cases of brain tumors were also found as were 13 cases of lung cancer. These represented 320 and 60% excesses above the expected frequency of these cancers, respectively. A 100% excess in deaths due to suicides was also noted.

In addition to these overall cancer excesses, an increasing trend of cancer deaths with time was observed. No excess deaths due to cancer were observed prior to 1965. However, in the period 1965-69 about a 50% excess in total cancers was observed and in the period from 1970 and later a 100% excess in total cancer deaths was found.

This trend is generally consistent with the clustering in recent times of reported occupational cases of liver angiosarcoma.

These data infer that at least two other forms of cancer, lung and brain, in addition to liver cancer, are increased among vinyl chloride workers. The present analysis did not examine the absolute risk of death in the study population, which conceivably could be less than in the general population. However, the observed excesses in specific cancers combined with the time trend for all cancers was considered by the authors to suggest a relationship between exposure to vinyl chloride in the work environment and cancer at multiple sites.

Nicholson et al. utilized Union and Company records to identify a cohort of 257 individuals each with a history of occupational exposure to vinyl chloride in a polymerization plant for at least 5 years subsequent to 1946.[15] This cohort included all individuals employed in this plant during the period 1946-1963. The mortality status of these individuals was evaluated from the tenth anniversary of their employment through April, 1974. The minimum 5-year exposure criterion was established to focus upon the effects of significant durations of exposure. Beginning observations after only 10 years or more since onset of first exposure was meant to emphasize the possible long term effects of vinyl chloride. The majority of individuals in this cohort, however, were exposed to vinyl chloride for a period of 20 years or under.

This cohort represents a relatively young group since over half of the men were under age 37 when they entered the cohort. Over half of the men are presently employed in the PVC production facility though not all in locations with vinyl chloride exposure.

Of the 257 individuals in this cohort, 255 or 99% were successfully traced and their current health status evaluated. The majority of these men were directly employed in production although maintenance men and non-production workers were also included. Thus exposures varied considerably among study subjects. Unfortunately no measurements of actual exposures were available and no effort to consider exposure in the data analysis was made except for the exclusion from this cohort of those individuals employed exclusively as plant guards or outside the reactor and dryer buildings. Over half of the workers, however, reported experiencing symptoms of dizziness, headache or euphoria during work periods and 14 had experienced episodes of loss of consciousness. Accordingly, the authors concluded that peak vinyl chloride exposures may often have exceeded 1,000 ppm and may have occasionally approached 10,000 ppm in this production facility.

Included among the 24 deaths identified in this cohort were 3 confirmed cases of angiosarcoma of the liver. Despite the limited observations, the excess in total mortality and in deaths from cancer in this group (presumably compared to the white male U.S. population) is unusual in view of the relatively short period of followup. These preliminary findings suggest an excess in all deaths of 25% and a 131% excess in all cancer deaths though in neither case did these excesses reach statistical significance. In addition to liver angiosarcoma, one brain cancer and 2 lymphomas were observed, causing the authors of this study to consider, in view of the rarity of these cancers, a possible relationship between VCM exposure and effect.

A study of mortality and morbidity among current and past employees at two vinyl chloride polymerization facilities was conducted by the

National Institute of Occupational Safety and Health.[2] The criteria for selection of these study facilities were in order of decreasing priority: (1) involvement in the polymerization of vinyl chloride for at least 15 years; (2) existence of a sizable work force; (3) location in a state where vital status ascertainment would be facilitated; and (4) existence of an inhouse medical program.

Since cancer often takes many years to become clinically evident, the study population was restricted to individuals with 5 or more years employment and at least 10 years since onset of employment in departments directly involved in polymerization of vinyl chloride. The study population consisted of 930 white males. Followup of study members was endeavored from the time of employment termination to December 31, 1973. Unfortunately, 285 individuals (31%) were not successfully followed up, and it is unknown how the mortality experience of these people compared to those who were successfully traced. All individuals not successfully traced were considered to be alive and were included in the analysis, thereby making any findings of increased mortality in this study cohort a conservative estimate of risk. Comparisons between observed risk of death in the study population and expected risk based upon mortality rates for the general white male population of the United States were made. Measurements or estimates of previous exposure levels to VCM were not included in this study--an important limitation.

A total of 109 deaths were observed among these polymerization workers compared to 105 which would have been expected. Though this difference

is not statistically significant, it is still noteworthy since most occupational groups have a favorable mortality experience compared to the general population. Any deaths in the 31% lost to followup would, of course, have increased the observed number of deaths even more. An evaluation of specific causes of death indicated that, except for cancer, causes of death in the study group did not differ from those expected in the general population. However, a statistically significant ($P < 0.01$) 57% excess in cancer deaths above that which would have been expected was observed. This excess could increase as the status of those lost to followup is ascertained. Within this cancer category, excess deaths were not limited to any single organ system, excesses being observed for cancers of the respiratory system, blood forming tissues, and the brain and central nervous system. Deaths due to liver cancer in this population were almost 12 times above the expected number, and brain cancer deaths were increased fivefold. These latter contrasts were statistically significant ($P < 0.01$ and $P < 0.05$, respectively). It is not stated whether excesses in liver cancer besides angiosarcomas were observed. The majority (25/31) of observed cancer deaths in this study population did not occur until at least 15 years following first exposure to vinyl chloride.

Shown in Table 7.3.4 / is a comparison of the NIOSH mortality study with other mortality studies conducted by Tabershaw/Cooper Associates, the Mount Sinai School of Medicine, the Dow Chemical Company and Harvard University. It is evident that the results of all studies are reasonably consistent and together suggest an overall excess in cancer mortality among workers exposed to vinyl chloride for long durations. Both the NIOSH and Mt. Sinai

Table 7.3.4 A COMPARISON OF MORTALITY STUDIES AMONG VINYL CHLORIDE WORKERS

Comparison	Study				
	Tabershaw/Cooper[10,11]	Dow[12]	NIOSH[2]	Mt Sinai[15]	Harvard[13,14]
Number of Plants	33	1	2	1	2
Study Population					
a) Yrs. exposed	1 yr or more	1 yr or more	5 yrs or more	5 yrs or more	No Restriction
b) Onset since first exposure	No restriction	No restriction	At least 10 yrs	At least 10 yrs	No Restriction
c) Size of cohort	8,384	522	930	257	--
d) No. successfully followed up	7,128 (85%)	505 (97%)	645 (69%)	255 (99%)	--
e) No. of deaths	352	88	109	24	161
SMR's or Relative Risk					
All causes of death	75	91	103	126	--
All cancers	110 (total) 114 (only those with 5 yrs or more exposure)	84 (total) 250 (only those with high exposure with at least 15 yrs after onset of exposure	157**	231	150*
Multiple cancer sites suggested	Yes	Yes	Yes	Yes	Yes
Angiosarcoma of the liver found	Yes	No	Yes (?)	Yes	Yes

* Statistically significatn at $p < 0.05$

** Statistically significant at $p < 0.01$

studies which employed the same study criteria also suggest a disfavorable overall mortality experience among these workers, but neither comparison shows statistically significant differences in this regard. It is noteworthy that in each study, workers exposed for 5 or more years to vinyl chloride had greater than expected frequencies for all cancers ranging from 41-150% excesses; however, in only two studies were these excesses statistically significant at the 0.05 level or lower. The close similarity of these studies to the animal toxicology data also showing multiple organ involvement in carcinogenicity is worthy of note.[9]

In evaluating these observed mortality effects among vinyl chloride workers it must be recognized that the workplace situation may include exposures to other carcinogens and/or liver toxins in addition to vinyl chloride and that any one of these may have contributed to the observed effects. While this situation makes it difficult to draw final conclusions with regard to the role played by vinyl chloride in the development of liver cancer it is noteworthy that toxicologic studies in mice, rats and hamsters have observed liver angiosarcoma following inhalation exposures to vinyl chloride at concentrations of 50 ppm and higher.[9,16,17] The liver angiosarcoma lesions observed in these animal studies combined with the observations in industry strongly imply that vinyl chloride is related to liver angiosarcoma in man.

Most, but not all, cases of liver angiosarcoma to date have been detected among workers involved in the production of polyvinyl chloride from the vinyl chloride monomer. These workers may have been exposed to concentrations of vinyl chloride monomer in excess of the old threshold limit value (200 ppm TWA, 500 ppm ceiling) at some time in the past and it could be argued from these data that vinyl chloride does not produce liver

angiosarcoma in man except at these higher (> 200 ppm TWA) exposures.

In support of this position is the fact that liver angiosarcoma has not been reported to occur in workers employed in Southern and Southwestern United States VCM and PVC production plants. These facilities are frequently located outdoors and hence would result in lower levels of exposure to VCM than found in indoor plants. Further, the possibility must be considered that additional chemicals other than vinyl chloride, such as perhaps other halogenated hydrocarbons or trace metals, may have contributed to liver angiosarcoma in some workers.

On the other hand, a relatively small number of workers were employed in the VC/PVC production industry in the 1940's and consequently a sufficiently large number of individuals at all plants may not have been exposed for adequate durations to allow detection of effects in a disease with a long latent period. An adequate period of time may also not have elapsed since the onset of exposure to permit the emergence of effects among workers from all plants making VC or PVC at this point in time. Most plants in which liver angiosarcoma has not been observed began production of VCM or PVC in 1950 or later.[18]

7.3.2

Accordingly, the limited period of observation following onset of exposure among most vinyl chloride workers combined with the long latent period generally required before clinical evidence of disease is considered the most likely explanation for failure to observe liver angiosarcoma in workers employed at all plants particularly those in the Southern and Southwestern United States. Of 12 Southern or Southwestern VCM plants for which data are available, only one was in operation prior to 1950.[18] Of 8 Southern or Southwest PVC plants currently in operation for which there are available data, only one was in operation prior to 1950.[18]

With respect to levels of vinyl chloride exposure required to produce liver angiosarcoma, most, but not all, occupational cases reported to data have occurred among PVC workers and consequently may generally have involved TWA exposures in excess of 200 ppm with peak excursions in excess of 1,000 ppm. The most definitive evidence for past exposures among these workers comes from actual 8-hour average air measurements ranging from 120-385 ppm and excursions of 2,000 - 4,000 ppm among highly exposed PVC workers at the Dow Chemical Company from 1950-1959.[19] Evidence of peak exposure excursions in excess of 1,000 ppm among PVC workers in past years is also derived from the frequent reports of neurological symptoms among such workers. Existence of odors attributed to VCM for much or part of the workday at these plants would tend to support these observations since the odor threshold for vinyl chloride is believed to be 250 ppm or higher.[20]

Reports of liver angiosarcoma among workers exposed to VCM but not involved in the production of PVC, however, including that of an accountant in a U.S. vinyl cloth plant would tend to argue that at least for some individuals, liver angiosarcoma may occur at much lower exposures than encountered among PVC workers. Cases of liver angiosarcoma are reported in a worker employed at

7.3 - 22

a VC monomer plant in Sweden and in a worker from England employed at a vinyl cloth plant.[2] Data from the Dow Chemical Company[19] show TWA exposures at monomer plants in the years 1973-1974 to generally be under 10 ppm although short-term exposures in excess of 100 ppm have been reported. A survey by the National Institute of Occupational Safety and Health has shown VCM levels in fabricating plants to range from 1-12 ppm.[21]

In the case of workers at fabricating plants, vinyl chloride exposures may result in part from release of trapped monomer in the PVC during processing and/or from inhalation of PVC dust containing entrapped monomer. While it is difficult to reconstruct exposures to vinyl chloride in these instances, it is likely that exposures for the workers involved in the fabrication process are considerably less than those for workers involved directly in the production of the monomer or the polymer.

In addition to the carcinogenic effects of vinyl chloride, a considerable body of evidence has become available related to non-malignant, effects in man including reactions of the liver to vinyl chloride. The vast

majority of evidence in this regard comes from observations among industrially exposed individuals. In reviewing these studies of non-malignant effects among individuals exposed to vinyl chloride, several criteria for evaluation were established. Included among these criteria were the following:

-- Were control group comparisons made either with workers not occupationally exposed to vinyl chloride or with members of the general population? If control group comparisons were included, how closely were these groups matched to exposed individuals?

-- Were important covariates considered among exposed and control groups such as age, sex, race, alcohol intake, drug intake, exposure to other toxic chemicals either in previous or present occupations or in the non-work environment, age at time of first exposure, latent period since onset of exposure and duration of exposure?

-- Adequacy of physical examinations and laboratory tests. Were physical exams performed? What laboratory tests were employed? Are laboratory test specific for injury caused by vinyl chloride? Were biochemical tests performed in the same laboratory and at the same period in time? How adequate were quality control procedures in and among performing laboratories? What were the cutoffs between normal and abnormal laboratory findings? And were these consistent? Were duplicate tests run?

-- Adequacy of exposure estimations. Was exposure actually measured or was it estimated? If exposure was estimated, how? If exposure was based upon job categories, were factors such as age of the plant, and type of plant (process and whether indoor or outdoor) considered?

It is recognized in establishing evaluation criteria such as listed above that no single study could possibly consider every important factor. This is particularly true with respect to many of the recent studies which were performed in an effort to obtain as much possible information in the shortest period of time. These criteria are useful in examining conclusions drawn from existing studies and in identifying gaps in knowledge that might appropriately be addressed in future studies. All of the studies discussed in this regard are lacking in at least one important area.

Evaluation of the acute effects from vinyl chloride were carried out by Lester et. al in 1963, who reported on animal and human acute toxicity experiments with VCM.[22] Three men and three women were exposed for 5 minute periods twice each day, separated by a 6-hour interval, for three successive days to vinyl chloride concentrations up to 20,000 ppm. Acute toxic effects were observed at concentrations above 8000 ppm (dizziness, nausea, dulling of visual and auditory cues, headaches, etc.). Follow-up examinations of these subjects have not been performed to determine whether or not such exposures produced any conceivable long-term, irreversible effects.

Kramer and Mutcher[23] correlated clinical and environmental measures for workers exposed to vinyl chloride for periods up to 25 years. The study population consisted of 98 healthy male workers. Exposure indices for these men were based upon actual air measurements at Dow since 1950 and expressed as cumulative dosage (ppm-years) and career time weighted averages considering the time each worker spent in critical job classifications. Ninety-five parameters of history, physical examination and laboratory tests were studied among exposed individuals and comparisons were made with workers

in other departments who had examinations during the same period of time. Of 21 clinical parameters under study, 6 showed significant correlations ($P < 0.05$) with exposure variables, cumulative TWA and cumulative dose. These significant parameters were systolic and diastolic blood pressure, BSP retention, icterus index, hemoglobin and beta-protein. The best correlation was between exposure and BSP retention (coefficient of multiple determination, 0.4). Based upon these observations the authors considered the possibility that ".... repeated exposure to vinyl chloride at TWA levels of 300 ppm or above for a working lifetime together with a very low level of vinylidene chloride may result in slight changes in certain physiologic and clinical laboratory parameters. The possibility of some impairment in liver function tests must be considered even though no overt clinical disease was evident in any of the individuals studied."

It is noteworthy that a good dose-response relationship between BSP retention and career TWA exposure was observed over the entire range of exposure examined. Based upon the derived regression equation BSP retentions of 12.5% were expected among those with TWA's of 300 ppm and 5.6% among those with TWA's of 100 ppm. A BSP rentention in excess of 5%, is considered to be abnormal in clinical medicine and suggests that substantial damage to liver cells may have occurred.[24] Judging from the data as presented, a small fraction of individuals with career TWA's of 50 ppm had abnormal BSP retention tests suggesting that liver damage had occurred. Exposure to other liver toxins such as alcohol was not adequately considered in this study.

Observations of liver damage, among workers who fabricate PVC plastic into finished products as well as among workers who convert VC monomers into the polymer indicate that injury to the liver among exposed workers is important and that such damage may occur at lower levels of exposure than is usually encountered in the production of PVC. In studies from Germany, enlarged livers and spleens as well as abnormal tests of liver function were found in PVC production workers.[25,26] Liver histology from specimens obtained during laparoscopy revealed evidence of liver pathology in a high percentage of cases. These workers had a history of employment ranging from 1½ to 21 years but no measures of past vinyl chloride exposure were available and it is not known whether adequate comparisons were made with control groups.

Following these initial reports of liver damage in PVC production workers from Germany, additional studies were carried out in 50 individuals with varying durations of exposure to vinyl chloride during the production of PVC.[27] These studies indicated that there was a relation between the duration of exposure to vinyl chloride and the severity of liver damage as determined by histologic examination of biopsy specimens. The most severe evidence of liver pathology was observed for workers with an exposure history in excess of 10 years.

Two cases of liver angiosarcoma were observed among these 16 German workers with a history of exposure to vinyl chloride

of 10 years or more and all workers in this category exhibited evidence of liver abnormality. Among workers with exposure durations of three years and under, all were found to have some form of liver damage, though the severity of damage was generally less than found in workers with greater durations of exposure. Of note is that all 5 workers examined who were not directly involved in the polymerization of vinyl chloride showed signs of minimal damage to the liver parenchymal cells. These observations coupled with reports of hepatomas in animals exposed to vinyl chloride suggests that liver parenchymal cells may be damaged by vinyl chloride.[17]

Although these studies do indicate a relationship between exposure duration and histologic evidence of liver damage, the lack of exposure data on these workers makes it difficult to determine what levels of exposure may have been responsible for such damage. Failure to compare exposed workers with a suitable control group not exposed to vinyl chloride and failure to consider the effect of alcohol intake are other limitations which deserve mention.

Examinations of 70 out of 128 workers in a PVC production plant revealed evidence of extensive abnormalities based on biochemical indicators and other tests.[28] These workers were employed an average of 7.7 years in the industry (range 6 months to 21 3/4 years). Upper abdominal complaints were present in 42 of 70 workers and symptoms such as tiredness, dizziness, parasthesias and arthralgia were frequently reported. Thrombocytopenia, increased BSP retention, and splenomegaly were present in a majority of cases, 81,67 and 57% respectively. Reticulocytosis was also common (41 %) and abnormal liver enzymes, esophageal varices and leucopenia were also observed. Unfortunately, effects of exposure, both level and duration were not evaluated in this study. Further, the frequency of abnormal findings among workers

not exposed to vinyl chloride was not studied so that it is difficult to accurately judge the effects of such exposure. Findings such as splenomegaly, thromborytopenia and increased BSP retention in the majority of instances does, however, suggest that damage in excess of the expected frequency among the general population had occurred in these workers though these changes were not necessarily specific for vinyl chloride.

To assess the possible implications of these findings, additional studies were carried out among workers in Germany employed in PVC processing plants. Such workers would have had a somewhat lower exposure than those involved in the direct polymerization of PVC from the monomer though they would be exposed to vinyl chloride as for example during rolling and shaping operations particularly when heat was required. Medical examinations were conducted among 15 such workers who were employed an average of 5 years, ranging from 1½ to 13 years.[29] Seven of these workers complained of pressure and/or pain in the upper abdomen. Thrombocytopenia and increased BSP retention (a test indicating abnormal functioning of the liver) were found in 7 of 15 workers though not necessarily concommitantly. One worker was observed to have an enlarged spleen. Of 4 workers in this group who underwent laparoscopy and liver biopsy, one showed histologic evidence of liver damage similar to, though less severe than, that observed in PVC production workers.

Though comparable control groups were not examined, the similar histologic damage in one worker to that found in PVC production workers suggests that lower level exposures to vinyl chloride (unfortunately not measured) may also cause liver damage.

Some, but not all, investigations carried out in the United States also observed liver damage among workers exposed to vinyl chloride. At the B.F. Goodrich plant at Louisville, Kentucky, for example, 1183 employees had blood tests to screen for evidence of liver damage. These workers included individuals involved in other than the direct production of PVC such as maintenance personnel, administrators and secretaries. On an initial screening test (SMA-12), 315 of 1183 or 26.6% showed at least one abnormal blood test and 41 or 3.5% had 2 or more abnormal tests. Among the 315 tested for a second time, 75 had a persistent abnormality. The most common observed abnormality in this test was an elevated alkaline phosphatase although increased bilirubins and SGOT's were also observed.

Based upon this initial battery of screening tests, 116 individuals were given more extensive blood tests which indicated the presence of some abnormalities in 59 or about 50% of those examined. Seven of these individuals had major abnormalities which required additional procedures. The highest percentage of abnormal batteries (10.9%) occurred among PVC production workers, although abnormal batteries were also found in other production workers, in maintenance workers and in non-production workers such as clerical personnel.

Depending upon results from the battery of tests, more elaborate diagnostic procedures such as liver scans, hepatic arteriograms and liver biopsies were initiated. Of 17 individuals undergoing such tests, 11 cases of portal fibrosis, indicating severe damage to the liver were uncovered, Two of these cases occurred among workers not directly involved in the production of PVC raising the possibility of damage at relatively low levels of exposure. In 2 of these 11 workers, both involved in PVC production,

angiosarcoma of the liver was found.

While this study in Louisville did document evidence of damage related to vinyl chloride; i.e. liver angiosarcoma, it is not at all clear from this study, the extent to which less severe liver damage may or may not be related to vinyl chloride. Although there is suggestive evidence that less severe damage may also have occurred, adequate comparisons were not made with matched control groups, and measurements of vinyl chloride exposure were not made. Accordingly, level of exposure could not be related to observed effects. Failure to correlate abnormal tests with duration of exposure or with latent period since onset of exposure, and lack of consideration of alcohol intake are additional limitations in this study.

Studies carried out in a PVC production plant in Niagara Falls did consider several of the factors not examined in Louisville; i.e. duration of exposure and alcohol intake but unfortunatley did not measure exposure directly. In this instance, a total of 354 workers were examined, 267 of whom were currently employed in a vinyl chloride polymerization plant encompassing nearly the entire work force. Also examined were 87 former workers. Hepatosplenomegaly was observed in a high percentage of current and formerly exposed workers (15.0 and 3.4% respectively) with the most frequent occurrence in each category among workers exposed for 20 or more years. Though hepatosplenomegaly was generally less frequent among former workers, in present workers hepatosplenomegaly was observed among 6% of workers with a history of exposure not greater than 2 years' duration and there was a

sharp increase in this abnormality among workers exposed for more than 5 years. Nearly one-third of current workers exposed for 20 or more years showed enlarged livers or spleens. Though hepatosplenomogaly was generally higher in each exposure category among those with a history of significant alcohol intake compared to those with no significant intake, in each group, the frequency of hepatosplenomegaly was related to duration of work exposure. Abnormal tests of liver enzymes were also present even among those with exposures of not more than 2 years' duration and these abnormalities were generally more frequent with increasing duration of exposure. It is of note that elevated alkaline phosphatase, the most frequently observed biochemical abnormality, did not correlate well with ethanol intake but did correlate significantly with duration of exposure to vinyl chloride. In addition to finding evidence of liver involvement in these workers, abnormal tests of pulmonary function and abnormal chest X-rays were also associated with increasing durations of exposure to vinyl chloride.

While the relation of abnormal findings with duration of exposure suggests an effect related to vinyl chloride, failure to compare these results with the frequency of abnormalities in a matched control group not exposed to vinyl chloride is an important limitation. Without such information it is difficult to evaluate the true significance of these findings.

As noted above, not all U.S. studies observed effects among workers exposed to vinyl chloride. One such "negative" study involved an evaluation of health surveillance data on 335 workers with industrial exposures to

vinyl chloride at the Dow Chemical Company.[32] This survey was based upon a multiphase screening program that had been available to employees at Dow since 1967. The study population was comprised of production employees who had worked for at least one year between 1942 and January 1972 in areas with potential vinyl chloride exposure who were also employees of the Dow Midland Division between February 1967 and March 1974, the period of the multiphasic health screening program.

Exposure categories were based upon industrial hygiene data that had been compiled from 1950 and later using estimated time weighted average concentrations for an 8-hour day. The high exposure group was defined as those with exposures above 200 ppm for a duration of one month or longer; the intermediate group had exposures from 25 to 200 ppm; and the low group had exposures under 25 ppm. A fourth exposure category, undefined, was established for those individuals for whom sufficient industrial hygiene data was not available. A subjective evaluation indicated that most individuals in this latter group were exposed in the low to intermediate range. The participation rate in the multiphasic screening program was about 80% in all exposure groups.

The availability of measured exposure data for most of these workers provides a much more objective evaluation of past exposure levels than is available from most other industrial studies. However, it should be noted that by giving precedence to a period of one month's high exposure in defining the highest exposure group, this category may have included individuals with predominantly low level exposures throughout the majority

of their work experience. On the other hand, the lowest exposure category would not have included workers with a history of high level exposure to vinyl chloride.

Because of revisions in the multiphasic screening program in 1970, the data obtained before and after this date were analyzed separately. A control group of matched pairs for sex, age, smoking history and month of exam and where possible date of hire was included in the analysis. The parameters studied prior to 1970 included tests of pulmonary function, blood pressure, white blood count, total bilirubin, SGPT and alkaline phosphatase. The only statistically significant difference ($P < 0.05$) between exposed and matched pair control groups was for decreased diastolic blood pressure in the high exposure group. No differences between exposed and control groups were noted in terms of pertinent historical questions including shortness of breath, chronic cough, jaundice, gastrointestinal trouble, numbness in hands or feet, cancer, anemia or blood problems.

The health surveys conducted from January, 1971, included similar historical information and laboratory tests for pulmonary function, hemoglobin, white blood count, SGOT, LDH, total protein, protein albumin and protein globulin. Statistical analysis of alkaline phosphatase was not performed due to changes in laboratory procedures. No statistically significant differences between exposed and control groups were found.

The availability of measured exposure data and the comparability of laboratory results with the inclusion of matched pair controls for each exposure category in this investigation overcomes many of the important

shortcomings in other available studies. Lack of information as to possible toxic chemical exposure in the matched pair controls and failure to consider the impact of duration of exposure to vinyl chloride are, however, important shortcomings in this study. By defining the study population as those who had been exposed to vinyl chlordie for at least one year without further considering the impact of duration of exposure, the exposed groups may not have included a sufficient number of individuals with longer durations of contact with vinyl chloride to necessarily be manifest in effects. A major addition to this study would have been the inclusion of clinical data based upon physical exams and additional laboratory studies both of which, however, are planned for the future. Based upon the available date the author concluded "....below 200 ppm nothing of statistical significance has been observed." It is, however, considered unlikely that the high exposure group was really exposed to TWA exposures of 200 ppm over the lifetime of their employment since high exposures of only one month's duration were sufficient to plase an individual into this category. As noted above, an earlier study at Dow suggested that liver damage may have occurred among some workers with TWA exposures of 50 ppm.[23].

Kotin reported the results of a study of currently employed workers exposed to vinyl chloride at Air Products and Chemicals, Inc. facilities as well as the results of a death certificate survey of PVC employees who had left the company or died while employed at the company. Plants at Calvert City, Kentucky, and at Pace. Florida were included in this survey. A detailed medical history was taken on each employee examined and physical exams with X-Rays and laboratory procedures were performed including tests of liver function.

7.2.3

At Pace, Florida, 13 of 201 employees examined were found to have abnormal findings. Persistent minor abnormalities were found on retesting of 3 employees but these were not considered sufficient to justify further immediate retesting although retesting 90 days later was scheduled. The remaining 6 employees were given liver scans, all of which were normal. One case of acroosteolysis was found at Pace, Florida.

At Calvert City, Kentucky, tests were performed on 291 employees, 97 of whom showed an abnormality on initial testing, partly due to equipment malfunction. Following retest, 29 employees showed persistent abnormalities, 16 of which were considered equivocal, not justifying further immediate additional testing but indicating retesting 90 days later. Among the 13 employees who were immediately retested, 6 showed findings indicating the need for further laboratory and physical exams. Of these, 2 cases of Gilbert's disease, and 2 cases of gallbladder disease were found, including one with coexistent hepatitis. An additional case of chronic persistent hepatitis without gall bladder disease was found.

Examinations of the death certificates did not indicate any relationship between exposure to vinyl chloride and cause of death.

In light of these results, except for the one case of aeroosteolysis the authors concluded that there was no evidence to identify vinyl chloride as a causative agent in disease. No cases of angiosarcoma were identified in this survey.

In presenting these data no indications are given as to how age, level and duration of exposure may have varied among these who were tested. No definition of what constituted an abnormal test was given and no effort

was made to contrast exposed workers to a comparable control group. Measurements of vinyl chloride exposure were not made nor is there any indication as to what percentage of workers examined were suspected to have high vinyl chloride exposures. The adequacy of followup among workers who had left the plants with respect to the death certificate survey is similarly not indicated, and no data are presented as to the frequency of abnormal findings on physical exams, particularly enlarged livers and spleens. While it is encouraging to note that no cases of angiosarcoma were observed, careful followup of these workers would appear indicated, particularly since both plants under study were opened in the late 1950's.[18]

Accordingly an adequate latent period following onset of first exposure may not have been present to allow effects such as liver angiosarcoma to be evident.

A survey of 36 PVC plants was conducted to determine if there were factories in which no cases of liver angiosarcoma were observed despite the presence of adequate exposure to vinyl chloride to have caused disease as defined by time and concentration.[20] Plants in which angiosarcoma had occurred were not included in the analysis. Similarly plants with operating experiences of 10 years or less were also discarded from the analysis. The remaining 16 plants included 2,372 persons currently employed and 1,471 previously employed, not all of whom had durations of exposure long enough to be manifest in angiosarcoma. Included among these individuals, however, were 787 persons who had worked more than 10 years and 104 persons who had worked more than 20 years with vinyl chloride. Also included were

1,402 persons with a time lapse since first vinyl chloride exposure of more than 10 years and 416 persons with a time lapse of 20 years or more.

Of these 16 plants only 2 had conducted measurements of vinyl chloride concentrations prior to 1970. Accordingly, the presence of vinyl chloride odors was used to estimate past exposures. The odor threshold for vinyl chloride is in the vicinity of 250 ppm though it may be much higher. On this basis 4 companies indicated that vinyl chloride odors were detectable for most of the work day prior to 1960; only 2 of 16 plants reported odors most of the day between 1960 and 1970 and no plants reported odors this frequently after 1970. However, all 16 plants reported the occasional presence of vinyl chloride odors at some time in the past although this was never considered to be a rare event, particularly prior to 1960. In view of these observations, exposure to time weighted average concentrations of vinyl chloride were considered to have exceeded 50 ppm in recent years and 250 ppm prior to 1960.

Since January 1, 1974, 3,285 examinations were conducted on employees in these companies including 872 retirees. This constitutes a follow-up rate of nearly 90% of all employees, but only 60% of those who were previously employed. Of these men, 3,249 were given liver profile tests as included in the SMA-12, i.e. bilirubin, SGOT, LDH and alkaline phosphatase. An abnormality in one of these four tests was reported in 15% of those examined, but this fell within the levels of abnormality observed among 900 Union Carbide employees not exposed to vinyl chloride and 400 office personnal with no known occupational chemical exposure. Similarly, the

occurrence of abnormalities in 2 tests (2.7%) and in 3 tests (1.3%) were comparable to those found in control groups. No mention is made of reports of findings on abnormal physical exams. In making these comparisons, no information is given as to the makeup of vinyl chloride exposed compared to control groups particularly with respect to covariates that may have affected test results. Similarly no definition of an abnormal test is given and there is no information as to quality control efforts among the various laboratories participating in these tests.

Based upon these observations the author concluded that "Examinations of these men have failed to show the existence of abnormal liver function tests in greater proportion than would be found in a control population. There is no case of angiosarcoma of the liver among these 1,402 men even though their exposure time is sufficient for disease to have occurred...." In drawing this conclusion, however, it should be noted that only 104 individuals had worked more than 20 years with vinyl chloride and 416 individuals had a time lapse since first exposure of 20 years or more. This would seem important since, of the 19 worldwide reported cases of angiosarcoma among PVC workers for which details are available, 15 had a time lapse since first exposure of 15 years or more and 14 had 15 years or greater exposure to vinyl chloride.[2]

Considering the lack of information on control and exposed groups and the many laboratories participating in these analyses, it appears difficult to draw any conclusions with regard to the frequency of abnormal liver function tests among these vinyl chloride workers. The fact that only 60% of former workers who may have had the greatest durations of exposure were included in these examinations of liver function tests is a serious shortcoming, as is failure to examine the influence of duration of VC exposure upon abnormal liver function tests.

A summary of the data showing non-malignant effects of vinyl chloride is shown in Table 7.3.5. The results of these studies and their limitations have been discussed above.

These observations of liver injury among PVC workers and particularly among workers not directly involved in PVC production, have potentially important implications with respect to the health of the general population exposed to vinyl chloride. In reviewing these findings it is, however, important to recognize that other toxic agents either work or non-work related, such as liver toxic drugs or alcohol could have contributed to many of these abnormal findings. Further, some of the biochemical screening tests are not specific for liver injury, though others such as BSP are. Ideally, one would like to know the prevalence of liver injury among comparable non-industrially exposed populations before drawing final conclusions regarding the effect of exposure to vinyl chloride upon the liver from the above studies. Most studies were lacking in this regard. In spite of difficulties with the present studies such as noted above, there

Table 7.3.5

SUMMARY OF OCCUPATIONAL FINDINGS RELATING
NON-MALIGNANT LIVER DAMAGE TO VINYL CHLORIDE EXPOSURE

Study Group (Number studied)	Level of Exposure	Duration of Exposure	Observed Effects
PVC Production workers [25,26]	Unspecified	1½ to 21 years	Enlarged livers and spleens Abnormal BSP retention Biopsy of liver showed portal fibrosis
PVC Production workers [45] liver biopsy study[27]	Unspecified	a) 3 years and under b) 10 years and more	a) Biopsy showed mild liver damage in all workers b) Relation between duration of exposure and severity of damage with most severe liver pathology observed in workers with 10 or more years of exposure
Post - PVC polymerization workers[5] -- liver biopsy study[27]	Unspecified	Unspecified but likely exposed to lower levels of VC than workers involved in polymerization process	All 5 workers examined showed evidence of mild damage to liver parenchyma based on liver biopsy
PVC Production workers -- [70,28]	Unspecified	6 mos to 21 3/4 years (average 7.7 years)	Upper abdominal complaints, lethargy and parresthesias common complaints Thrombrytopenia, increased BSP retention and splenemegaly found in majority of workers
PVC Processing workers [15,29] not involved in PVC polymerization but exposed to PVC as a finished product and hence by inference exposed to lower levels of vinyl chloride than PVC production workers	Unspecified	1½ to 13 years	7/15 workers complained of pressure or pain in upper abdomen Thrombrytopenia in 7/15 workers Increased BSP retention in 7/15 workers Biopsy showed mild liver damage similar to that in PVC production workers

Table 7.3.5 (Continued)

Study Group (Number studies)	Level of Exposure	Duration of Exposure	Observed Effects
PVC Production workers, and non-PVC production workers (1183 total) [30]	Unspecified	Unspecified	116/1183 or about 10% showed significant biochemical abnormalities; abnormal liver function tests found in non-PVC production workers 11 cases of portal fibrosis found on liver biopsy, 2 of which were in workers not directly involved in PVC production
Current and former PVC production workers (354 total) [31]	Unspecified	a) ≤ 2 years	a) Hepatasplonomegaly observed in 6% of workers exposed not more than 2 years
		b) 5-10 years	b) Sharp increase in hepatasplonomegaly in workers exposed greater than 5 years
		c) 20 years or more	c) Nearly one-third of workers exposed 20 years or more had hepatosplenomegaly Elevated alkaline phosphatase correlated with duration of exposure Abnormal lung function tests found
PVC Production workers (98) [23]	TWA exposures up to 300 ppm	Up to 25 years	Abnormal liver function (BSP retention) correlated with TWA exposures -- Evidence of abnormal BSP retention at TWA exposures of 300 ppm and suggestive evidence of BSP retention in some workers exposed to TWA of 50 ppm
PVC and non-PVC production workers (335) [32]	TWA exposures of 25-200+ ppm	1 year and greater	No adverse effects related to angiosarcoma
PVC workers (492) [33]	Unspecified	Unspecified	One case of acro-osteolysis only evidence of injury attributable to VC
PVC workers (3,843) [20]	Estimated as greater than 250 ppm prior to 1960	Includes exposed 20 years and more	No increased abnormalities above levels in control groups

is suggestive evidence presented for at least minimal liver damage associated with vinyl chloride which may be observed with durations of exposure under 2 years. Though there is reason to believe that cessation of exposure to vinyl chloride would cause a reversal in some of this damage; there is also evidence that in some people, this damage is not fully reversible and may even progress further. For example, one vinyl chloride production worker examined by liver biopsy at the National Institute of Health showed persistent and perhaps progressive liver pathology 2½ years after the cessation of exposure despite an absence of abnormalities in biochemical tests of hepatocellular function.[34] There is also concern that the histologic changes in the liver observed in PVC workers may represent pre-malignant changes that would increase the risk of developing angiosarcoma in future years.

Any final conclusions regarding the implications of these findings for the general population who are exposed to levels of vinyl chloride in the air generally much lower than in occupational situations must await completion of additional studies. However, several observations do suggest that exposure to vinyl chloride in the air may pose some risk to health at these lower levels.

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7.4 Ecology

The potential problems associated with release of vinyl chloride into the environment are just coming under scrutiny. For sometime it has been known that the plastic, polyvinyl chloride is not biodegradable. Microorganisms are not able to utilize the plastic or are able to do so only after an extended period of weathering. Although acetylene and ethylene are both capable of being reduced by microbial activity,[1,2] their chlorination seems to make them less amenable to attack by microorganisms. Available evidence does indicated that alkenes may be oxidized by heptone grown pseudomonas species.[3] Very little is known regarding the biological metabolism of alkynes.[4]

The fact that polyvinyl chloride is not readily biodegradable has led to the difficulties attendant with the disposal of this form of plastic . Incineration has been the chief means of disposal; however, this method is not without its problems. Hydrogen chloride is generated in the normal burning of refuse even when plastics are not present.[5] During burning, most of the chloride present in refuse and in the polyurethane and polyvinyl chloride materials, which were added to the base refuse in the test work, was evolved as hydrogen chloride. No free chlorine gas or phosgene was detected. Though hydrogen chloride is evolved when burning refuse, the amounts released do not compare to those released when polyvinyl chloride and polyvinylidene chloride plastics are incinerated. Addition of polyethylene and polystyrene plastics to normal base refuse containing no plastics had no effect on chloride ion emissions because

these plastics contain no chlorine. Addition of polyurethane foam resulted in slight increases up to 689 parts per million (0.0689%) when a 2% addition was made to the base refuse and 751 parts per million (0.075%) when 4% was added. Adding polyvinyl chloride to the normal refuse increased chloride ion emission to 1990 parts per million (0.1990%) for the 2% addition and to 3030 parts per million (0.3030%) for the 4% addition.[5]

The effects of hydrogen chloride gas on vegetation have been known since the mid-nineteenth century when damage was noted in the vicinity of alkali plants in Europe and Great Britain.[6] The concentration of hydrogen chloride in stack gases was limited to 0.45 mg/m^3 in 1874. No further reports of crop damage due to this gas occurred after the passage of the Alkali Act of 1906 in Great Britain. Damage due to hydrogen chloride gas has been reported in the United States by Weiler,[7] Hindawi[8] and Wood.[9] Antipov[10] reported hydrogen chloride gas damage to ornamental plants near a chemical factory in the USSR which released fumes once or twice a month. Species which were affected included oriental poppy, daisy, belleflower, columbine, bluets, and pylox. The study by Wood is the only one which specifically reported the combustion of polyvinyl chloride as the source of the hydrogen chloride gas. The smoke from the combusion of polyvinyl chloride insulation at a wire salvage operation in northern Pennsylvania caused extensive damage to several northern hardwood species.

Bohne[11] reported hydrogen chloride gas damage to shrubs, trees and flowers near a hospital incinerator.

Not all plants are sensitive to hydrogen chloride gas. Means and Lacasse [12] tested the sensitivity of 12 coniferous and broad-leaf tree species to hydrogen chloride gas. The fumigations were conducted under controlled conditions at a temperature of 27 C, relative humidity between 78 and 85%, and a light intensity of 1.4×10^4 ergs/cm^2 sec. Under these conditions the only symptom noted on conifer needles was a tip necrosis on white pine at 8 ppm, on Douglas fir at 12 ppm, and on Norway spruce at 19 ppm. Austrian pine and arborvitae were not injured at concentrations of 18 and 43 ppm respectively. Symptoms on broadleaf species included marginal and interveinal necrosis and necrotic flecking. Tulip poplar was injured at 3 ppm, European black alder and black cherry were injured at 6 ppm, and sugar maple and Norway maple were injured at 7 ppm. Red oak was not injured at concentrations up to 13 ppm. These fumigations were also of four hours duration.

The effects of hydrogen chloride gas on vegetation has not been studied in any detail. This probably reflects its unimportance as a phytotoxicant. Hydrogen chloride gas is easily scrubbed from flue gases and the major sources are point sources; therefore, it has not been emitted into the atmosphere in large amounts. The incineration of chlorine-containing plastics in large amounts could change this picture.

Studies showing the effects of vinyl chloride in the environment are extremely scarce. A study by Heck and Pires [13] in 1962 indicates that vinyl chloride can cause significant injury to plants. An analysis of the results using five different fumigants at three different levels

ranked them in the following order. ethylene > acetylene > propylene > ethylene oxide > vinyl chloride. Table 7.4[1] compares the five compounds and indicates the levels at which they were most toxic.

The injury symptoms shown for acetylene, propylene and vinyl chloride were identical to that shown by ethylene. Ethylene is usually considered as a physicologically active gas rather than a toxic gas, e.g. sulfur dioxide. Ethylene affects a great number of physiological phenomena in plants, such as ripening of fruits, abscission of plant parts, proliferation of tissue, inhibition of growth and variations in cellular metabolism.[14] Ethylene is a product of plant metabolism, but vinyl chloride has not been reported from natural sources.

The effects of vinyl chloride upon microorganisms have not been studied. As mentioned previously, there has been little work done to determine whether alkynes can be metabolized by microorganisms.[3] Ethylene is taken up by soil;[15] vinyl chloride may be also.

A by-product of vinyl chloride production, EDC-tar, has been disposed of by dumping into the North Sea. EDC-tar is a mixture of short-chained aliphatic hydrocarbons. When it is dumped into the ocean, it gradually sinks toward the bottom. As the tar sinks, the components gradually dissolve in the water. Therefore, its sedimentation rate is low. It also has a tendency to adhere to a large variety of substances and form a film or layer around the particles. Plankton are among those particles to which the tar adheres.

Studies by Jernelov, Rosenberg and Jensen[16] indicate that marine animals rapidly accumulate EDC-tars from contaminated sea water. An accumulation factor of 2900 was estimated for shrimp (Leander adspersus) exposed to 0.01 ppm EDC-tar for 48 hours. The accumulation of low molecular weight

Table 7.4.1 COMPARISON OF THE TOXICITY LEVELS OF THE THREE CONCENTRATIONS OF FIVE FUMIGANTS ON ALL PLANT SPECIES[1]

Toxicity level[2]	Fumigant	Concentration (ppm)
1	Ethylene oxide	1000
2	Ethylene	10, 100, 1000
	Propylene	1000
	Acetylene	1000
3	Acetylene	100
	Vinyl chloride	1000
4	Acetylene	10
5	Propylene	100
	Ethylene oxide	100
	Vinyl chloride	100
6	Propylene	10
7	Ethylene oxide	10
	Vinyl chloride	10

[1]Plants were fumigated for 7 days in each fumigant at each concentration.
[2]A qualitative comparison with 1 causing the death of all plants and 7 showing no effect.

compounds of EDC-tar is highest via water, whereas the high molecular compounds show the greatest accumulation through the food chain. These conclusions are in agreement with the results of studies dealing with Cl-C compounds such as DDT seawater. Dieldrin has also been shown to accumulate rapidly through solution and much less slowly through the food chain.[16] When compared to DDT, PCB and other Cl-C aromatic substances, the biological half-time is short (1 day to 3 weeks). This fact may mean that the effects of ECD-components might not be as severe as those of DDT, PCB's and other chlorinated hydrocarbons.

Studies made to determine the effects of EDC-tars on different stages in the life cycle of the barnacle Balanus balanoides L.[17] showed that the stage II nauplii were ten times more sensitive than the older stage V and VI larvae. Age, therefore, seems to make the barnacles more tolerant to the EDC-tars.

In an attempt to determine some physiological aspects of EDC-tars at the cellular level, the microorganism, Escherichia coli was studied.[18] The death of the intact cells was shown to be due to the breakdown of the permeability of the cytoplasmic membrane. The authors suggest that since most known biological membranes are formed according to similar principles, the action of EDC-tar on the cell membranes of higher organisms would be similar.

7.4.2 Summary

Polyvinyl chloride plastics are not readily biologically degradable. This has led to incineration as a means of disposal. Incineration of polyvinyl chloride plastics results in the emission of hydrogen chloride gas. Hydrogen chloride gas is injurious to plants, but emissions can be readily

controlled.

Vinyl chloride is damaging to plants. Injury to plants from vinyl chloride is similar to that caused by ethylene; however, no extensive studies have been made.

The effects of vinyl chloride on microorganisms has not been studied nor have the capability of microorganisms to metabolize it. Ethylene is taken up by soil; vinyl chloride may be also.

EDC-tars, a mixture of short-chained aliphatic hydrocarbons, are a by-product of vinyl chloride production. When dumped into sea water, they show a tendency to be rapidly accumulated by marine animals. The low molecular weight compounds have the greatest accumulation.

In Escherichia coli the death of intact cells was shown to be due to the breakdown of cytoplasmic membrane permeability. It is suggested that because all biological membranes are formed according to similar principles, the action of EDC-tar on the cell membranes of higher organisms would be similar.

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7.5 VINYL CHLORIDE IN PERSPECTIVE

The compelling evidence for the carcinogenicity of vinyl chloride from both an epidemiological and toxicological standpoint raises the question of the possible carcinogenicity of other related chemicals in the ambient air. The possibility exists of multiple exposure to a host of compounds that may act additively or synergistically to produce a hazardous health effect.

Available data do not allow quantitative evaluation of the hazard of multiple exposures. Published data, however, suggests that compounds similar in metabolism to vinyl chloride which may appear of minor importance when only low dosages of individual substances are considered, could become more important from a health standpoint when total multi-compound dosage is evaluated.

7.5.1 Industrial Production and Use of Chemicals Related to Vinyl Chloride and Polyvinyl Chloride

Structures, production figures and major uses for chemicals of industrial importance with structure similar to vinyl chloride and polyvinyl chloride are summarized in Table 7.5.1.

7.5.2 Carcinogenicity of Chemicals Related to Vinyl Chloride and Polyvinyl Chloride

The publication "Survey of Compounds which have been tested for Carcinogenic Activity"[3] was used as the primary source of information on the following chemicals:

1. 1,1-Dichloroethylene (vinylidine):

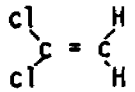
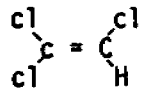
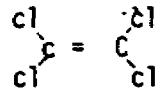
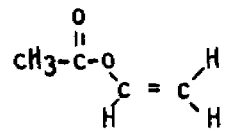
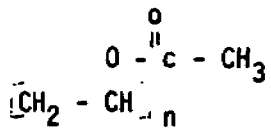
   No data has been published.

2. 1,2-Dichloroethylene:

   No data has been published.

TABLE 7.5.1

PRODUCTION AND USE IN THE UNITED STATES OF CHEMICALS
RELATED TO VINYL CHLORIDE AND POLYVINYL CHLORIDE

Chemical	Structure	Production (Million Pounds)	Major Uses
1,1-dichloroethylene (Vinylidine Chloride)		—	Monomer for Vinyl Chloride Copolymer and Polyvinylidine Chloride
Trichloroethylene		438(1972)[1]	Metal Degreasing, Manufacturing Solvent
Tetrachloroethylene (Perchloroethylene)		745(1972)[1]	Dry Cleaning, Metal Degreasing, Chemical Intermediate
Vinyl Acetate		729(1969)[2]	Polymer Production
Polyvinyl Acetate		422(1970)[1]	Textile Sizing, Adhesives, Paper Coating, Polymerization Aid
Other Vinyl Polymers (Alcohol, Butyral and Formal)	———	219(1970)[1]	———

3. Trichloroethylene[4]

Several animal species have been exposed to levels from 200 to 3000 ppm for up to six months with follow-up observations up to nine months. No tumors were observed in any animals.

4. Tetrachloroethylene (Perchloroethylene)[5]

Various animal species were exposed for seven hours a day to 100-2500 ppm for up to 250 days with no tumors discovered.

5. Polyvinyl Chloride[6]

Film was implanted in various locations in rats for up to eighteen months. Several tumors were observed, but all were in the area of the implant.

6. 1,1,2-Trichloropropene[7]

Rabbits were dosed orally with compound in oil at 0.1 LD_{50} for 6 months. There was evidence of changes in lymph nodes after 18 months.

7. Vinyl Alcohol Polymer[8]

Implants of polymer sponges at various locations in rats for the life span of the rats gave many sarcomas at the site of implantation and a few tumors at other locations..

8. Vinyl Chloride Acetate Copolymer[9]

Implants in rats gave formation of tumors only at the site of implantation.

For the most part, toxicological studies of chemicals related to vinyl chloride have been limited to acute studies with only minor emphasis on long term or carcinogenic effects. When carcinogenic studies were undertaken they were, in general, of insufficient exposure duration or involved too limited a number of animals to provide conclusive negative results in this regard.

7.4.3 Other Carcinogens in Polluted Community Air

The array of contaminants identified in polluted community air includes other chemical and physical agents which are either proven or highly suspect carcinogenic hazards such as polycyclic aromatic hydrocarbons, azaheterocyclic hydrocarbons, certain metal compounds, asbestos and certain radionuclides.[10,11] However, very few definitive studies have been conducted to determine the contribution of these ambient pollutants to human carcinogenesis. One of the observed epidemiologic characteristics of the worldwide increase in lung cancer is the higher incidence in urban residents. Although there are other factors which may contribute to urban and rural differences such as population density and occupational differences, an urban-rural difference in lung cancer rates persists even after correction for these factors. Additional support for a probable etiological role for ambient chemical carcinogens in lung cancer can be gained from several studies undertaken to measure the effects of population migration on lung cancer risk.[12-14]

These studies in migrants have shown that either increases or decreases in lung cancer are compatible with changes in environment. The changes in rates parallel the general population concentrations in the areas under study and persist after correction for cigarette smoking, although at a reduced level. Moves from high pollution to low pollution regions reduced lung cancer death rates and vice versa (Table 7.4.2). Within the United States and the United Kingdom studies show a gradient of risk to lung cancer from low in rural to high in urban areas. Migrants from rural to urban areas in the United States appear to increase their lung cancer rates.

In a recent article,

Paul Koten draws attention to certain observations on the nature of carcinogens which should be considered when initiating studies of carcinogenesis associated with air pollutants.[15]

1. Cancer induction most frequently requires prolonged periods of exposure to carcinogenic agents.
2. Cancer can be caused by several carcinogenic agents acting in combination either in an additive, synergistic or inhibitory relation to one another. This is particularly relevant to lung cancer where a variety of ubiquitous environmental exposures to carcinogenic agents exist.
3. The action of a carcinogenic agent in lung cancer induction may be determined by the competency of the host's defenses at the anatomic, physiological and biochemical levels. Polluted community air contains a large variety of chemical and physical irritants, which though unable to cause cancer, facilitate the action of carcinogenic agents by attenuating or destroying the effectiveness of muco-ciliary apparatus of the lining of the lung. This facilitates deposition and retention of particles carrying carcinogenic agents. In addition, these irritants can induce changes in the epithelium (metaplasia) which may enhance the progression of changes to cancer. These irritants may alter the metabolic handling of carcinogenic agents and thereby enhance their cancer inducing potency.
4. There is evidence that at the cellular level, environmental chemical co-factors of a highly non-specific nature may work together with chemical carcinogens to increase their effectiveness.

TABLE 7.2

AGE ADJUSTED DEATH RATES FROM LUNG CANCER IN GREAT BRITAIN, NORWAY, AND THE UNITED STATES

Population Group	Lung Cancer Death Rate (Per 100,000 Persons) Males	Females
Great Britain residents	151.2	19.3
Great Britain born U. S. residents	93.7	11.5
Norway residents	30.5	5.6
Norway born U. S. residents	47.5	10.7
Native U. S. residents	72.2	9.8

It would be wrong to consider vinyl chloride as an isolated situation, but rather it should be viewed as an example of just one of many potential chemical carcinogens which may be present but as yet unidentified as carcinogens. This suggests that more attention be given to the detection of other chemical carcinogens in the myriad of industrial chemicals to which the general population is exposed either as individual compounds or as multiple exposures.

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7.5.4

8 CONTROL TECHNOLOGY AND REMEDIAL ACTIONS

8.1 INTRODUCTION

Most of the presently used or available technologies are a basic part of the processing system and serve to recover reactant or product. These controls are appraised herein using performance data from the manufacturing plants, or by comparing emission levels for plants with and without controls. Controls so appraised for VCM production include: recycling of vent streams, condensation with refrigeration, adsorption with carbon, incineration, oxidation with ozone, absorption (scrubbing), and venting to flares. Monomer loading and unloading involves special additional controls: vapor collection adapters with recycling, thermal level detectors with recycling, and magnetic gages. Polymer production can possibly benefit from consideration of controls indicated for the monomer production, plus vacuum stripping, steam stripping, and the recycling of carrier air streams.

A qualitative assessment of the potential applications of selected controls has been made based upon information presented to date by U.S. industrial firms. The results of this assessment are summarized for each process in the following paragraphs. All percent reductions of emissions are estimates.

8.2 MONOMER PRODUCTION

The relatively scarce data seem to point to a present total emission of about 90 kg/million kg of VCM produced. To this amount should be added a smaller, intermittent loss of VCM in the loading area.

A 90 percent reduction can be obtained by refrigeration and/or absorption of vinyl chloride in the vents by appropriate solvents (EDC for instance) and by combustion of the organics in other vent streams, followed by removal of HCl produced. A 90 percent reduction is about at the limit of present-day technology. For such a reduction the loading area must be policed for vent losses.

8.2.1 VCM From Acetylene and HCl

The reactor vent is the main emissions source, accounting for 60 percent of total emissions. Condensation at 44 °C (40 °F) and 0.29 X 10^5 N/m^3 (35 Psig) is now used. Addition of refrigeration would decrease emissions by about 50 percent. If an HCl scrubber were also used, the combined controls should achieve 85 percent reduction. These, combined with carbon adsorption, should reduce emissions 99 percent. Recycling, incineration, oxidation with ozone, and venting to flares do not appear to be applicable.

Fugitive emissions equal about 25 percent of total emissions. Use of diaphragm valves, replacement of packed pump seals with pressurized mechanical seals, use of vapor collectors on samplers, and preventive maintenance can be expected to reduce these emissions by 50 to 95 percent.

Tank-car loading accounts for an estimated 15 percent of emissions. Incineration, with HCl recovery should reduce condenser vent loses 99 percent. Thermal level detectors combined with vent gas refrigeration and/or recycling would reduce slip gage emissions by 95 percent. Replacing the slip gages with magnetic gages could reduce the emissions nearly 100 percent. Vapor collector adapters with recycling would reduce purge losses 50 to 90 percent. Incineration should reduce loading air emissions about 90 percent.

8.2.2 VCM From Addition Reaction of Chlorine to Ethylene in Air Atmospheres Followed by Dehydrochlorination

Major emission sources are of VCM from the EDC light ends column vent (9-20 percent) the heavy ends tar removal column vent (18 percent), the VCM light ends column vent (10-13 percent), and tank car loading (10-20 percent).

EDC light ends column emissions could be reduced about 50 percent using refrigerated condensers and nearly 100 percent with carbon adsorption. Recycling to a post chlorination unit would be almost 100 percent effective.

Heavy ends column emissions are believed to be controllable by incineration (50 percent reduction), and by adsorption (close to 100 percent reduction).

VCM light ends would require adsorption or oxidation with ozone, both capable of nearly 100 percent reduction.

Tank car loading controls given in Section 8.2.1 would apply here also.

8.2.3 VCM From Addition Reaction of Chlorine to Ethylene in Oxygen Atmosphere should be Followed by Dehydrochlorination

Major emission sources of VCM and their controls are believed to be essentially the same as described in 8.2.2. The use of oxygen would reduce the quantitative amounts of vent streams from the EDC product processing, and thus would of itself reduce emissions somewhat.

8.2.4 VCM From Direct Chlorination and Dehydrochlorination of Ethylene

The controls are essentially the same as described in Section 8.2.2 and would have about the same range of efficiency. This process must avoid HCl emissions by recovering it for other usage. Incineration with HCl-recovery by scrubbing is about 90 percent efficient for this purpose.

8.3 POLYMER PRODUCTION

In the production of polyvinylchloride, present monomer losses in kg/kg of product are at least an order of magnitude higher than in the production of VCM. Most producers report about a 3 to 4 percent lower PVC production

than monomer intake. Fr m some data submitted by manufacturers, 1 to 1.5 percent of PVC made is lost. A portion of this is emitted as fine particulated to the atmosphere. The actual monomer emission is therefore in the order of 2 to 3 percent. These losses result from the batch nature of the polymerization operation and in the filtration and in the drying of the polymer, if practiced. Reduction of these losses poses a more difficult if not an impossible problem. To indicate the severity of the problem, a direct reduction to 50 percent of the present level of losses seems possible, but a 90 percent reduction of the emissions in some of the existing polymer plants without process changes might be beyond present techniques at acceptable costs. However, if intensive stripping of the suspension at the end of the reaction is allowable, the 90 percent reduction might be feasible at acceptable costs.

One development should be noted, namely the move to progressively bigger reaction vessels. One company has studied and is proposing use of a 45.4 m^3 (120,000 gal.) polymerization reactor compared to the present typical size reactor of 19 to 38 m^3 (3,000 to 10,000 gal.) A possible emergency blowing of such a reactor might, however, lead to very high peak values of vinyl chloride emissions.

This report has not considered the influence of VCM remaining in the polymer. This residual monomer, sometimes present to about 1000 ppm, is mostly released during further processing and might thus create emission problems during fabrication processes, particularly those involving heat.

8.3.1. Suspension Polymerization

Fugitive emissions throughout the process account for an estimated 45 percent of VCM emissions. The emission sources must be better defined before specific controls can be discussed. However, a good maintenance program and minor equipment modifications should reduce fugitive emissions by about 50 percent.

Vacuum stripping of the crude product would be 50-80 percent efficient for reducing emissions from the blend tank which accounts for about 11 percent of the total emissions. Carbon adsorption would reduce this source 50 to 99 percent; condensation with refrigeration, 50 to 70 percent; incineration, 50 to 99 percent; absorption, 50 to 80 percent.

Collectively, vents from the dryer, the air conveyor, the storage site, and wash water provide 35 percent of the total emissions. Vacuum stripping and absorption are expected to give 50 to 80 percent reduction and recycles to compressors, 40 to 60 percent reduction in emissions from these sources.

8.3.2 Emulsion Polymerization

The dryer vent, air conveyor vent, site storage vent, and waste water vent appear to account collectively for about 85 percent of total emissions. Carbon adsorption, oxidation with ozone, and steam stripping could reduce these emissions by 50 to 99 percent. The recycle of air streams could be 40 to 80 percent efficient. Fugitive losses contribute 7 percent of the emissions; blend surge tank vents contribute another 7 percent. Vacuum stripping, if practiced would effect 50 to 80 reduction; carbon adsorption, 50 to 99 percent. Condensation with refrigeration would reduce either source about 40 to 60 percent. Absorption is expected to reduce both losses 50 to 80 percent. Preventive maintenance would reduce fugitive losses 25 to 50 percent. The surge tank vents could be recycled giving 40 to 60 percent reduction, or they could be oxidized with ozone to provide 50 to 99 percent reduction.

8.3.3 Bulk Polymerization

The VCM reactor vent (25 percent) fugitive emissions (35 percent), and the combined resin receiver, collector, and storage (20 percent) are the major emission sources. For the reactor vent, adsorption (50 to 90 percent reduction), oxidation with ozone (90 percent reduction), and incineration (50 to 90 percent reduction) are indicated for control purposes. Intensive maintenance is believed to be capable of giving

50 to 75 percent reduction of the diverse and ill-defined fugative emissions which need further study. The product collection systems vents could be water-washed, then adsorbed (50 to 90 percent reduction), oxidized with ozone (90 percent reduction), or incinerated (50 to 90 percent reduction).

8.3.4 Solution Polymerization

While no data are at present available for this process, it is expected to have the emission characteristics of the suspension process (section 8.3.1) and to respond roughly to the same controls.

8.4 RESEARCH AND DEVELOPMENT UNDERWAY

Allied Chemical is developing a technique for controlling hydrocarbon emissions from the oxychlorination process. Control of vinyl chloride is expected to be a side benefit of this work.

Industrial R&D groups are investigating the use of carbon sorption and solvent scrubbing as gas stream cleaning techniques. They are also trying to develop a more porous polymer form which will facilitate stripping of the monomer from the polymer.

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APPENDIX A

ESTIMATES OF RISK FROM LOW LEVEL EXPOSURE TO CARCINOGENIC CHEMICALS

Several statistical models have been developed for extending observed response associated with several exposure levels (dose-response curves) determined in experimental animals to undetermined response dosages below those used experimentally and extrapolating these theoretical considerations to estimate risk to human health with regard to low level exposures to carcinogenic agents.

The estimated risk associated with exposure to vinyl chloride based upon animal experiments has been presented using several of these models and the available toxicologic dose-response data.[1]

Mathematical Models

Models available for estimating risk associated with exposure to carcinogenic agents fall into two main categories, i.e.those that deal with tumor incidence as a function of dose and those that deal with latent period modification as a function of dose (exposure level). Several models designed to predict response beyond the limits of available experimental data have recently been reviewed.[2-8] Strategies for assessing risk range from those that place emphasis on safety factors and best scientific judgement to those that involve statistical extensions beyond the limits of observed response data.[4-7] Among the important factors to be considered in the use of these models are the following:

Any exposure to a carcinogen may be associated with a certain degree of risk. This risk is expressed with regard to a particular carcinogen. However, multiple exposures to several carcinogens and non-carcinogenic synergistic agents in general are not considered in these models.

None of the available models have been adequately confirmed by direct experimental studies at the very low end of the dose-response relationship. Since these models represent extrapolations beyond the limits of available scientific data, they should not be construed as "scientific dogma."

Linear models of a quantal biological response (all-or-none) are useful for selection of a mean effective dose. In estimating risk to the population, the slope of the extrapolation curve and the confidence level selected for estimating risk are extremely important parameters. The intrinsic reliability of these models depends upon proper experimental design with appropriate attention given to biologic factors that may modulate response. It is extremely important to note that linear models assume a no-threshold effect level, and the level of risk determined by the slope of the dose-response curve can be influenced greatly by the experimental design and the selection of the model used.

These models are as valid as the assumptions made in their design; e.g. it is assumed that the distribution of sensitive, cancer prone individuals in the population is represented by a normal (Gaussian) distribution.

A committee of scientists under the direction of the National Academy of Sciences, Advisory Center for Toxicology have recently reviewed biological and statistical considerations in assessment of risk. This review soon to be published (January, 1975) is presented here for those who desire a more in-depth discussion of these matters.[8]

CHAPTER V

SOME BIOLOGICAL AND STATISTICAL CONSIDERATIONS IN THE ASSESSMENT OF RISK

CONTENTS

V. SOME BIOLOGICAL AND STATISTICAL CONSIDERATIONS IN THE ASSESSMENT OF RISK

Applying the results of toxicological investigations conducted in the laboratory to the population of interest generally involves two kinds of extrapolations. The first, which is more difficult to deal with and more important with respect to human exposure, involves predicting the probable effects on one species from the results of experiments performed on another. The second kind of extrapolation is that of extending dose-response curves beyond the limited range of observation to determine the dose corresponding to an extremely low incidence of adverse effects on the organism tested.

A. THE ROLE OF THE TOXICOLOGIST IN THE ASSESSMENT OF RISK

This report concerns itself primarily with the task of developing objective technical information needed to make decisions on the course of action to be followed to insure the safe use of chemicals. It does not, except for a general statement of principles, go into the socio-political aspects of decision-making.

Terms such as "toxicological insignificance," "safe," "zero tolerance," "no effect level," and negligible risk" have been in rather common use. All of these contain in one way or another value judgments or technical implications which have no place in an objective assessment of risk. There is no substance which, under certain circumstances, cannot be dangerous and unsafe. There is no battery of tests, however elaborate, which can prove beyond challenge the complete safety of a chemical. For the toxicologist to apply the terms "toxicologically insignificant" or "negligible risk" to a set of observations makes a premature judgment in the wrong arena by the wrong person as to insignificance or acceptability. An attempt has been made to eliminate such terms from this report.

Another common term of wide usage is the "no effect level." This is statistically meaningless and therefore of limited value since it merely means that no effect was observed in studies using a group of animals of particular size. Such an observation is completely compatible with the presence of an adverse effect, which in further studies with larger sample sizes or with different types of observation might lead to a positive outcome. We prefer the usage of the term "no observed effect," which should always carry with it a qualifying statement as to size of the group in which no adverse effect was observed.

In most instances it will be imperative to develop a dose-response relationship, and because many toxicological techniques are relatively insensitive, high doses (which produce high incidence of effects) are frequently required. These can be and have been called "unrealistic" or "inappropriate." Such exposures may be well above, sometimes many orders of magnitude above, likely levels of exposures to human or wildlife systems. Nevertheless, they are often an essential part of practicable laboratory studies which necessarily use limited numbers of animals. The underlying challenge to the toxicologist is to use these points on the dose-response curve as a means of quantifying responses, and to devise, with suitable margins of safety, appropriate means for extrapolating to realistic, actual exposure conditions. The biological aspects of this extrapolation will be discussed first, and the statistical considerations will be developed later.

B. BIOLOGICAL CONSIDERATIONS

For clarity in the following, it will be assumed that we are concerned with extrapolation from the laboratory situation to human populations.

Except in the case of lifesaving drugs, only very low risks will normally be accepted in chemical usage. The acceptable risk will, however, vary with the benefit anticipated. In the case of risk of death from a chemical of trivial utility, the acceptable risk would be essentially zero. Put in explicit terms, this might mean 1 death in 100 million persons. As noted in the section on statistics below, extrapolation to such risk levels from experiments on small numbers of animals is extremely uncertain. Again, and as noted repeatedly in this report, the gravity of the effect is a major determinant in an overall assessment of risk. At one extreme lies a fatal outcome, and at the other, a temporary functional alteration producing no disability or discomfort and lying fully within the range of physiological compensation. The susceptibility of human populations varies widely since genetic background, age, prior or co-existent disease are all important determinants, and part of the toxicologist's task is to identify susceptible groups in the population as the basis for establishing limits of exposure.

Another and vital factor constantly facing the toxicologist is the often striking biological differences between the effects of chemicals on laboratory species and on man. It has been repeatedly shown that no one species (including non-human primates) has responses parallel to the human over a wide range of the effects of chemicals. The choice of species must then be based on a determination of the biological similarity in the responses to the chemical under study.

In extrapolating from animals to man the transfer is often made on a dose per unit weight (milligram per kilogram) basis. This practice overlooks the well demonstrated (Freireich et al., 1966) observation that dose per unit surface area (mg/m^2) is generally a better transfer parameter.

There has been much loose talk about "thresholds." The term threshold means "the entrance or beginning point of something." This implies (and is normally so used) a discontinuity in the slope of the dose-response curve. True discontinuities in biological phenomena are rare. However, they do occur. One example is the threshold for glucose excretion by the kidney. Most biological dose-response relationships appear to be smooth functions and in absence of concrete evidence dose-response curves should probably be assumed to be smooth. Many dose-response curves have an "S" shape with a much lower slope at the low end of the curve than in the mid-range. This could be regarded as a "quasi" threshold. The steepness of the dose-response curve is an important consideration for predictive purposes. A steep dose-response curve implies a sharp cutoff (again, a "quasi" threshold) with decreasing dosage.

Some dose-response curves appear to be linear, especially when attention is limited to relatively low incidence rates. One example of this is cigarette smoking and lung cancer (Doll, 1967); there are many experimental situation where this appears to be the case.

Despite the above comments, there are some biological reasons for anticipating that with some chemical agents there may be something approximating a true threshold. The biological basis for this is twofold: (1) the possibility of a relatively greater effectiveness of repair mechanisms at low dose levels; and (2) the possible presence of competing biochemical processes which could convert the chemical to harmless products at low dose levels. It is difficult to generalize on these mechanisms since they can be expected to depend on the chemical and the species. Unfortunately, investigation of these questions has rarely been undertaken.

In the past, these complex considerations have been dealt with pragmatically by the use of arbitrary "safety factors."

C. STATISTICAL CONSIDERATIONS

The need for a proper consideration of statistics in the design of toxicological experiments and in the interpretation of the results cannot be overemphasized. First, before meaningful results can be obtained, attention must be given to identifying and reckoning with possible sources of error. Second, statistical techniques are available which can give meaningful estimates of the level of exposure to chemicals corresponding to the level of risk which the decision-maker considers acceptable.

1. Experimental Error and Sampling Error

The outcome of an experiment is normally dependent upon innumerable factors, only some of which are known and even fewer of which are controllable. In dose-response experiments with animals, for example, some identifiable factors influencing the outcome include (1) the composition of the particular batch of test preparation, which typically represents a significant source of variation in independent repetitions of the experiment, (2) animal variability, (3) technician reliability, and (4) the precision of laboratory techniques such as dilution techniques or dose preparation. Since such factors influence the dose-response relationship, they represent sources of experimental error, and hence independent replications which randomly sample the levels of these factors are necessary in order

to estimate their contributions in the measure of experimental error. If major sources of variations are not considered in such replication, then statistical precision as reflected in the width of confidence intervals, for example, may be grossly misleading.

When several major sources of experimental error can be identified, a conceptually simple experimental design would consist of independent replicates at each target dose level randomly sampled with respect to all sources of variation. If batches from the chemical manufacturer represent a source of variation, for example, then this design might assign each animal at each dose level to a different batch of chemical from the manufacturer. If dilution errors are non-negligible, then dilutions to target dose should be independent, not only among dose levels but also among animals within dose levels. When several such sources of errors exist, this conceptually simple, completely randomized experimental design clearly becomes impracticable, and blocking becomes a more feasible means of conducting the experiment. Thus, each batch of the chemical from the manufacturer might be administered to a group of animals at every test dose to produce, in effect, a separate dose-response curve for each batch. For any one batch, the proportion of animals responding at a given test dose is subject to sampling error due to such factors as animal differences and possible errors in dilution which would result in each animal receiving a slightly different test dose. At any given dose level, the proportion responding also varies among batches; thus, the average proportion responding at a dose level is subject to both sources of error, namely, the sampling error within batches and the variability among batches, which together comprise experimental error. A valid statistical analysis should utilize the appropriate experimental error and not merely its sampling error component.

Since standard statistical methods of bioassay often are addressed only to the analysis of sampling error, there is need for caution in applying these methods.

2. Estimating Low Effect Levels

Estimation of low effect levels poses a difficult problem. Direct experimental estimation of the level affecting one percent of the population may require several hundred animals to obtain adequate statistical precision. For many reasons, particularly in human populations, much lower risks than one percent are desired. A true no-effect level cannot be observed experimentally. Any observed level has meaning only for a particular sample size.

The observation of no-effect for a group of animals may arise from one of two reasons: (1) the dosage level may indeed be below the theoretical no-effect level; or (2) the number of animals tested may have been inadequate to give a high enough probability of detecting a biologically important change. For example, a test on 20 animals may show no deleterious effect, but a test on 100 animals, tested under the same conditions, may show one or more animals exhibiting deleterious effects. Similarly, for a graded response, a small sample may fail to provide enough statistical precision to detect a change from baseline, whereas a larger sample may. Thus, an observed "no effect level" has no absolute meaning since it depends on sample size and poorly estimates the theoretical "no-effect level"; a better term would be the "no observed effect level."

However, data from experiments in which no effects are observed are useful in placing limits on the probable incidence of effects. For example, if no animals out of 100 animals displayed a deleterious effect, it can be stated with 99% confidence that fewer than 4.5% of animals tested under these conditions

would exhibit deleterious effects. If this level of risk is too high, more animals can be tested. For example, observance of zero animals affected out of 1000 tested results in an upper 99% confidence limit of only 0.46%. To reach an extremly low acceptable risk level in this manner generally requires a prohibitively large number of animals.

The past practice of selecting some arbitrary fraction of "no effect level" as a limit for exposure leaves one with no estimate of risk. However, a fairly conservative estimate of the risk can be made by employing the one-hit (one-particle) theory (Food and Drug Administration Advisory Committee on Protocols for Safety Evaluation, 1971). This theory states that for low dosages, if an experimental dosage is divided by a factor f, then its upper confidence level of the risk is also divided by the factor f. Such an approach will often result in near-zero dosages for extremly small acceptable risks. For example, if zero deleterious responses were observed in 450 animals at a dose d, it can be stated with 99% confidence that the true response rate is less than 1% (one out of 100). The predicted dose for risk of one out of 1,000,000 would then be $10^{-4}d$.

An alternate means of estimating low risk exposure levels involves extrapolation from parametric dose-response curves. Many different empirical mathematical models may be fitted to a set of experimental data (Finney, 1964). The probit and logistic curves have been commonly used in biology, for example, and both curves may fit equally well in the region of experimental observations (2% to 98% response range) but give widely different estimates for extapolated responses. For example, the probit curve will predict a dosage level approximately 140 times higher than the logistic curve for extrapolation to a dosage expected to elicit one response in 1,000,000 animals. In some instances

(Doll, 1967) linear dose-response curves have been reported; often, however, these cover only a relatively limited response range.

There is no assurance that the dose-response curve observed in the experimental range of dosages will apply at extremely low response levels. Mantel and Bryan (1961) suggest the use of a presumably conservative slope of one probit for each factor of 10 in dosage level for extrapolating to low levels of carcinogenic risk.

A more recent approach to the extrapolation of laboratory findings to the establishment of standards or limits for human populations (Albert and Altshuler, 1973) has taken into account age at the time of the appearance of the adverse effects as well as the frequency of its occurrence. In the case of cancer from external sources, for example, it has been shown, both experimentally and in humans, that with lower doses cancer appears later, that is, at increasing ages. Under this concept, and assuming the availability of reliable data, it should be possible to establish limits which would place the earliest occurrence of malignancy at an advanced age, e.g., no more than 10% incremental likelihood of cancer at age 95.

D. SUMMARY

In the past, toxicologists have not only made the laboratory assessments of toxicity, but in many instances they have made the final judgment as to the social course to be taken on the basis of a particular set of findings. Instead, the technical experts should be charged with securing an objective independent determination of the extent, nature, and frequency of adverse effects. They should be asked to explain the relative gravity of these effects for the target

system, be it humans or wildlife. Similarly, other qualified technical experts should be requested to make an objective assessment of the benefits of use and of alternative materials or processes. However, the final judgment as to a trade-off between an adverse health effect and a desired benefit is a social decision and should be made with the participation of those who are affected. This is not to say that technical experts using their technical expertise will not participate, but it does state that they should not be the sole judges of determining the balance between the benefit and the risk.

The dose-response curve is a valuable tool for assessing the safety of a chemical compound. Estimates of low effect levels are part of the information leading to the ultimate designation of safe and acceptable levels. The statistical problems of extrapolation from experimental dose levels to very low levels and the estimation of appropriate errors are particularly troublesome but can b handled if care is taken in the design and analysis of the experiments and the interpretation of results.

Without supporting experimental evidence, however, statistical analysis will never be capable of making the critical extrapolation from laboratory animals to man.

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APPENDIX B

THE HEALTH EFFECTS OF VINYL CHLORIDE

A Compilation of Toxicologic, Clinical, and Epidemiologic Data

SUMMARY OF TOXICOLOGICAL DATA
Human Data

Authors	Species	Sex	No.	EXPOSURE: Hrs. per Day	Days	Conc. ppm	Total Dose: ppm-Days	Observations	Pathology
Von Oettingen (1955)	Human					12,000 10,000 25,000		Dangerous Narcosis Produced symptoms of dizziness, disorientation, headache and burning sensation on soles of feet.	
Gabor Hecca-Radu Manta (1962) Chem.Abstract	Human		82	Workers exposed to DDT, Benzene, Hexachlorocyclohexane, VC, PVC				Blood: Decrease in catalase Increase in peroxidase, indophenoloxidase and gluthathione Changes occurred during second year of work.	None reported
Lester Greenberg Adams (1933)	Human	M F	3 3	Twice per day for 3 days; 5 min. sessions at 6 hour intervals	0 4,000 8,000 12,000 16,000 20,000	0 83.3 166.7 250.0 333.3 416.7		1/6 slightly dizzy 0/6 had any effects 1/6 slightly dizzy 2/6 definitely dizzy 6/6 dizzy, nausea, blurred vision and heaving symptoms stopped after exposure 6/6 intoxicated, one with persistant headaches 50% level of no effect is 1.3% No statement about repeated exposures	None reported
Gabor Radu Preda Abrudean Juanof Anca Valczkay (1964) Chem.Abstract	Human		78	PVC Workers				Decrease plasma albumin Increased β and γ globulin Decrease in β/γ for serum lipoproteins Decrease in serum cholinesterase Decrease in pseudo cholinesterase Normal blood catalase Normal serum pyruvic acid	None reported
Grigorescu Toba (1966) Chem.Abstract	Human			Experimental: PVC Workers Control: Other clinically healthy people				Hypothesis: $VC + H_2O$ > chloral + chloracetic acid (1). Results: (1) was found in 80% of exptl. people, but in none of controls. Most of + findings were in people exposed 2-5 years. In these cases, α - globulin is higher, β - globulin is lower than people with no (1) in urine. Capacity to metabolize (1) decreased after 2 years.	None reported

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SUMMARY OF TOXICOLOGICAL DATA
Human Data

Authors	Species	Sex	No.	EXPOSURE Hrs. per Day	Days	Conc. ppm	Total Dose ppm-Days	Observations	Pathology
...rris ...ars ...967)	Human		2	-	-	-	-		One worker had knee cap and toes involved in the acro-osteolysis. Other worker only hands.
...lson ...Cormick ...tum ...eech ...967)	Human	M	31	-	-	-	-	No cases of acro-osteolysis diagnosed in 1000 individuals who handled finished resin or used for plastic product production.	31/3000 (3%) workmen associated VC polymerization found to have acro-osteolysis.
								Age range of affected workers 26-47. Incubation period greater than 12 months of polycleaning experience.	22/31 Acro-osteolysis associated with Reynaud's symptoms.
...reeta ...ewart ...chler ...69)	Human	M	13	7.5	1	50 250 500	15.6 78.1 156.2	Breath decay curves, 0 to 20 hrs. after exposure were measured. Level in breath at 4 hrs. is ~ 1%. No adverse effects noted. About the same set of breath decay curves following occupational exposure.	None reported.
...ryautseva ...70) ...tract	Human	M F	50 43	-	-	-	-	1. Changes in ECG: rhythm, conductance, polarization. 2. Increase in systolic index.	None reported.
...la ...70) ...ublished	Human	-	1	8	1095			Acro-osteolysis symptoms, Reynaud's syndrome, aversion to fats, enlarged liver	Aerometry: [VC] on factory filters at air discharge time: 2,000 ppm [VC] at point of worker entry: 2,000 ppm in plants where acro-osteolysis occurred - 180 ppm (max) in plant with no disease [VC] on gangway and other parts of plant: 10 to 15 ppm.
			5	8	1825			Raynaud's syndrome	
			15		-			Enlarged liver, minor liver insufficiency.	
			500*					13/500 had acro-osteolysis. Olefactory threshold is 0.8 to 1%. Acute nervous symptoms become evident when it is easily perceptible.	

*In several other factories

SUMMARY OF TOXICOLOGICAL DATA
Human Data

Authors	Species	Sex	No.	Exposure: Hrs. per Day	Days	Conc. ppm	Total Dose ppm-hrs	Observations	Pathology
Dinman Cook Waterhouse Magnuson Ditcheck (1971)	Human		5011	21,51[illegible] Man-Years Experience				Conditions associated with hand cleaning of polymerizers. There appeared to be correlation between reactor deassing time and acro-osteolysis.	25 cases of acro-osteolysis. 16 other individuals questionable. Acro-osteolysis appears to be systemic rather than local disease. Reynaud's phenomenon was statistically related to acro-osteolysis.
Dodson Dinman Whitehouse Nasr Magnuson (1971)	Human	M	4	1-23 Months				All patients had worked as PVC reactor-vessel cleaners. Yes. Ca and P balance in one subject. Plethysmographic abnormalities were present in 3 subjects. Esophageal motility within normal limits. Catecholamine, 5-Hydroxyindole Acetic Acid excretion normal. All other numerous clinical laboratory investigations negative.	Reynaud's phenomenon anteceded osteolytic lesions in all four subjects. ^{18}F scintiscans correlated with radiographic lesions. No liver enlargement or hypothyroidism. Additional smaller abnormalities found in ulnar styloid, oscalcis and patella.
Kramer Mutchler (1971)	Human	M	98	- Up to 25 years Experience				Performed statistical correlation between several clinical measurements and total dose and time-weighted average VC concentration. 2 liver function indices show a positive correlation with total dose (abnormally high). a) Icterus index b) Bromsulphalein 3 other indices are dose-related but are not outside normal limits: a) systolic and diastolic blood pressure. b) hemoglobin negative correlation. c) beta-protein.	None reported.

SUMMARY OF TOXICOLOGICAL DATA

HUMAN DATA

thors	HUMANS Species	Sex	No.	Hrs/Day	Days	EXPOSURE Conc. ppm.	Total Dose ppm-days	OBSERVATIONS	PATHOLOGY
verson ier 372) stract	Human	-	1						Acroosteolysis Had unique popular skin lesions which have been described only in PVC workers
kowitz Donald chiere zner 72) stract	Human	-	-						Describes acroosteolysis symptoms. Incidence is <3% among workers
e ge in tman 73)	Human	-	13					Ages 29-52 Reactor cleaners 2-18 yrs. employment	Latent period: 1½-3½ years in 11 patients; 7 and 11 years in other 2 patients. Acro-osteolysis symptoms. Peripheral vessel changes. Thrombopeny (low count) is the first objective symptom described in all patients; lung fibrosis originating + portal system, large spleen, impaired lung function; 10% mortality. This is the first objective symptom described.

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SUMMARY OF TOXICOLOGICAL DATA
Human Data

thors	Species	Sex	No.	EXPOSURE hrs. per Day	Days	Conc. ppm	Total Dose ppm-Days	Observations	Pathology
steller bach ler e ze er man 73)	Human	-	120	1½ to 21 years.				20 PVC workers were studied out of 45 with suspected skin problems, because and possible to perform laparoscopy on 20. 30 to 56 years old.	Liver enlarged in 13/20. Pain in Rt. upper abdomen in 2/20. Hyperlipidemia has been diagnosed in 1967 after 6 years in 1/20. Jaundice history in 1955 before exposure in 1963, liver dysfunction was diagnosed, no alcoholism. Spleenomegaly in 7/20. Total bilirubin was > 1 mg/100 (which is upper normal limit) in 3/20. Bromsulphalein test was abnormal in 19/20 (>5% retention after 45 minutes). SGOT was > 12 mU/ml in 17/20. SGPT was elevated (15-30) in 14/20. Alkaline phosphatase was > 43 u/ml in 2/2 Hypothrombocytemia (<150x10³/mm³) was found 19/20, (<100x10³/mm³) in 12/2 Acro-osteolysis was seen in 4/20. Varicose veins of esophagus in 3/20. Liver histology: Collagen transformation of walls of sinusoids in 5/20. Focal activation of Kupfer cells in 9/2 Focal fatty infiltration in 14/20. Fibrosis of septa and capsule intralobular and portal spaces in 17/20. 15 additional blood parameters were normal. 9 immunological tests were done once, not repeated.

SUMMARY OF TOXICOLOGICAL DATA

ANIMAL DATA

Authors	ANIMALS Species	Sex	No.	EXPOSURE Hrs/day	days	Conc. ppm	Total Dose ppm-days	OBSERVATIONS	PATHOLOGY
Von Oettingen (1955) (Review Article)	Cats	ND	ND	ND	ND	ND	ND	VC is promptly excreted by lungs; 82% is eliminated after inhalation stops	
	Cats	ND	ND	<4	1	100,000 to 130,000	<1,200	Blood VC concentration reaches 15-17 mg%	
	Cats	ND	ND	<4	1	180,000	<30,000	This concentration causes sore intra-auricular pressure reduction as 13,000 ppm dichlorcethylene, 30,000 ppm ether	
	Cats	ND	ND	<4	1	200,000	<33,000	Cardiac insufficiency	
	Cats	ND	ND	4	1	250,000 to 300,000	<40,000 to 50,000	Even this does not produce complete cardiac failure	
	Cats	ND	ND	ND	ND	ND	ND	Blood levels are <40 mg% at time of cardiac arrest, 27-30 mg% at time of respiratory arrest	
	Rabbits Dogs	ND	ND	1min.	1	170,000	118	This is the narcotic concentration	
	Mice	ND	ND	1 min.	1	86,000 to 123,000	60 to 65	This is the narcotic concentration	
	Dogs	ND	ND	< 4	1	100,000	<12,000	Cardiac irregularities, ECG abnormalities	
	Dogs	ND	ND	3	7 for several wks	10,000	475	No major change in liver or kidney	
	Dogs	ND	ND	3	7 for several wks	200,000	9,500	Marked salivation, vomiting, respiratory arrest	
	Mice	ND	ND	10 min.	1	245,000 to 295,000	1,700 to 2,040	This is the lethal range for 10 minutes exposure	
	G. Pigs	ND	ND	short time	1	200,000 to 400,000	ND	All killed	

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Reference	Species	Sex	No.	Hrs/day	days	ppm	ppm-hrs	OBSERVATIONS	PATHOLOGY
Von Oettingen (1955) Review Article Continued	G. Pigs	ND	ND	0.5-1	1	100,000	2,000 to 4,000	Dangerous to life	
	G. Pigs	ND	ND	0.5-1	1	5,000	100 to 200	Higher concentrations than this cause severe lung edema and hyperemia of liver and kidney	
	G. Pigs	ND	ND	0.5-1		ND		Order of toxicity is: carbon tetrachloride > VC > ethyl chloride	
Pastrocatteo Fisher Christie Danziger (1959)	Mice	ND	5	0.5	1	100,000	2,083	Sequential effects were: 1. irritation, 2. increased motor activity, 3. twitching, 4. tremor, incoordination, 5. unconscious, 6. deep narcosis. All animals recovered in 8 minutes.	Mice: Light lung engorgement, kidney swelling. Rats and G. Pigs: same lung picture.
Fisher Christie Danziger (1960)	Rats	ND	5	0.5	1				
	G. Pigs	ND	5	0.5	1				
	Number of animals and duration of exposure same as above					200,000	4,160	1/5 mice died after 30 minutes, same symptoms as above but appeared sooner. Guinea pigs unsteady for 20 min. after exposure.	Lung engorgement, no edema in all species. One rat had fatty liver.
	Number of animals and duration of exposure same as above					300,000	6,250	5/5 mice and 5/5 rats died; 1/5 guinea pigs died; 4/5 guinea pigs recovered in 25 minutes.	Liver and kidney was congested, tracheal epithelium damaged
	Number of animals and duration of exposure same as above					400,000	8,330	2/5 guinea pigs died	Same symptoms, more severe
Torkelson (1) Oyen Rowe (1961)	Rats	M	10	7	(5d/wk (6.5%)	500	14,000	Growth and gross appearance were normal. Liver/body weight ratio and absolute liver weight larger than control in males. Liver/body weight and absolute liver weight not larger than control in females. Blood SGOT, SGPT, SDH, alkaline phosphatase were normal.	Central lobular liver degeneration. Kidney tubular damage.
		F	10	7					

Animal Data

Authors	Species	Sex	No.	Hrs/day	days	EXPOSURE Conc. ppm	Total Dose ppm-days	OBSERVATIONS	PATHOLOGY
Torkelson Oyen Rowe (1981) continued		M	5	7	(5d/wk 6.5mo)	0	0	Control animals	
		F	5	7					
(2a)	Rats	M	12	7	138 to exposures in 204 days (6.5 months)			All groups were normal in appearance, mortality and growth. Hematology (hemoglobin, hematocrit, cells) was normal. Liver function tests (SUN, SGOT, SGPT, alkaline phosphatase) were normal. All organ/body weight ratios normal except M and F rats, where liver/body weight ratio was increased.	Gross pathology was normal. Microscopic pathology was normal in all species except liver of M and F rabbits: Central lobular granular degeneration and necrosis.
		F	12	7					
	G. Pigs	M	10	7					
		F	8	7					
	Rabbits	M	3	7					
		M	3	7					
	Dogs	M	1	7		200	8,050 to 8,400		
		M	1	7					
	Matched controls, both exposed and non-exposed groups				5d/wk				
(2b)	Same protocols					100	4,000 to 4,200	All animals were normal in appearance, mortality and growth. Hematology (hemoglobin, hematocrit, cells) was normal. Liver function tests (SUN, SGOT, SGPT, alkaline phosphatase) were normal. Liver/body weight ratio of M and F rats were larger than controls.	Gross and microscopic appearance of tissues were normal.

Authors	Species	Sex	No.	Hrs/day	days	EXPOSURE Conc. ppm	Total Dose ppm-days	OBSERVATIONS
Torkelson / Oyen / Rowe (2c) (1961) continued	Rats	M	5	4	5d/wk for 6.5 months as above	200	4,600	Liver/body weight ratio larger than controls, not statistically significant.
		M	5	2		200	2,300	
		M	5	1		200	1,150	Liver/body weight ratio same as controls
		M	5	0.5		200	575	
		M	5	4		100	2,300	Liver/body weight ratio higher than controls, not statistically significant.
		M	5	2		100	1,150	
		M	5	1		100	575	Normal in all respects
		M	5	0.5		100	265	
(3)	Rats	M	24	7	130 exposure in 189 days			All parameters normal in all species.
		F	24	7				
	G. Pigs	M	12	7				
		F	12	7				
	Rabbits	M	1	7				
		F	3	7				
	Dogs	M	1	7				
		F	1	7				
	Matched controls, exposed and unexposed groups.							
Lester / Greenberg / Adams (1) (1963)	Sherman rats	ND	2	0-2	1	50,000	0-4,150	Moderate intoxication, righting reflex lost.
		ND	2	0-2	1	60,000	0-5,000	More intense intoxication, righting reflex present.
		ND	2	0-2	1	70,000	0-5,830	More intense intoxication, righting reflex lost.
		ND	2	0-2	1	100,000	0-8,330	Corneal reflex disappears, no gross pathology.
		ND	1	5 min.	1	150,000	552	Deep anesthesia.
				42 min.	1		4,383	Respiratory failure of same animal.
		ND	1	2	1	150,000	12,500	Deep anesthesia, complete recovery after exposure. No pathology observed.

SUMMARY OF TOXICOLOGICAL DATA
Animal Data

...thers	Species	Sex	No.	Exposure: Hrs. per Day	Exposure: Days	Exposure: Conc. ppm	Exposure: Total Dose ppm-Days	Observations	Pathology
...ster (2) ...enberg ...ns ...63) ...nt'd.	Sherman rats	M	9	8	2 then 13	100,000 then 80,000	Variable	After animal deaths, replacements were made in chambers. Two males survived all 15 exposures. Remaining animals and replacements survived an average of eight exposures.	
		F	9	8	Same exposures as above.			One died after two exposures at 100,000. One died after two exposures at 100,000 and three at 80,000. One died after two exposures at 100,000 and twelve at 80,000. Six/nine survived all fifteen exposures.	
		M	9	8		0		Control animals	
		F	9	8		0		Control animals	
								Growth stopped during exposures and resumed at normal rate after exposures.	Lungs had focal pneumonia which healed after two weeks of recovery from exposure.
								External appearance normal.	One-third of animals had parasitic cysts in liver.
								Liver color, appearance, consistency, degree of congestion was same as controls.	Liver pathology same as controls, but more variation in amount of fatty infiltration.
									Spleen had advanced lymphocytic hyperplasia.
									Kidney pathology same as controls.
(3)	Sherman rats	M	15	8	5 days/week for 3 months	20,000	434,000	1/30 died.	
		F	15	8		20,000	434,000	External appearance of all animals normal.	All organs had normal gross appearance.
								Liver larger, spleen smaller than controls.	Liver parasitic cysts in all animals.
								White blood cells lower, lymphocytes higher, neutrophils lower than controls.	Liver fat normal.
								Body weight and hemoglobin were same as controls.	No abnormal histology.
		M	15	8	Same	0	0	Control animals.	Congestion and swelling greater in liver than controls.
		F	15	8	Same	0	0	4/30 died.	Congestion and swelling less in kidney than controls.
									Congestion and swelling same in spleen as controls.

SUMMARY OF TOXICOLOGICAL DATA

Animal Data

Others	Species	Sex	No.	EXPOSURE: Hrs. per Day	Days	Conc. ppm	Total Dose ppm-Days	Observations	Pathology
ster (4) eenberg ams 553) nt'd.	Sherman rats	M	5	8	19	50,000	317,000	No mortality. On days 1-4, animals lost weight, showed neurological symptoms. On days 4-19, weight gain was normal. Serum transaminase, hematocrit, and prothrombin times were normal. White and red cell counts were lower than controls. Hair: all 5 males had thin hair and scaly tails; females and controls were normal. Liver/body weight ratio was higher than controls.	Gross organ appearance was same as controls. Liver pathology showed congested cells. Liver parasitic cysts seen in all animals.
		F	5	8	19	50,000	317,000		
		M	5	8	19	0	0	Control animals.	
		F	5	8	19	0	0	Control animals.	

SUMMARY OF TOXICOLOGICAL DATA
Animal Data

Authors	Species	Sex	No.	EXPOSURE Hrs. per Day	Days	Conc. ppm	Total Dose ppm-Days	Observations	Pathology
...uebler 1964) ...stract	Rats	ND	ND	2	100	5,000	41,600	No effect at 5,000 and 150,000 ppm.	No histological damage
	Mice	ND	ND	2	100	15,000	125,000	At 50,000, animals were hyperactive, but returned to normal after exposure.	
	G.Pigs	ND	ND	2	100	50,000	416,000		
	Mice	ND	ND	0.5 minutes		Distance 20-25cm	ND	Animals sprayed with a shellac-based hair spray	No change in lung histology
...zin ...okhova 1968a) ...stract	Rabbits	ND	ND	"chronic"		3,500 3,900	ND	Brain electrical activity changes: Appearance of beta waves (80 Hertz) in anterior and posterior hypothalmus along with circulatory changes.	
...zin ...okhova ...68b) ...stract	Rabbits	ND	ND	4	167 (5.5 mos.)	3,500 to 3,900	ND	Decreased heart rate, arrhythmia Decreased ECG voltage Decreased duration of systole Reduced blood flow. Increased arterial pressure.	Altered β waves in EEG from posterior hypothalmus. Potentials from anterior and posterior hypothalmus increased by 18-30% and 70-85% respectively.
...zin ...okhova ...969a) ...stract	Chin-chilla rabbits	ND	8	4	150	8 to 12	200 to 300	After 20 days, blood adrenaline rose from 3.5 μgm% to 6.15 μgm%; at 40 and more days, it was 6.6 μgm%. Posterior hypothalmus electrical activity also changed. This is the direct cause of hypertension.	
...zin ...okhova ...969b) ...stract	Rats	ND	ND		150 (5 months)			Disrupted cardiac work rhythm. Bradycardia and arrhythmia. Reduced relative duration of I-II and T-II sound intervals. Relative duration of QRS complex did not change. After 15 days recovery: cardiac activity rhythm returned to normal, but the duration of the sound interval remained below initial levels for another 15 days. Therefore, max. permissible VC concentration is significantly less than .03 mg/l (12 ppm).	

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SUMMARY OF TOXICOLOGICAL DATA
Animal Data

Authors	Species	Sex	No.	EXPOSURE Hrs. per Day	Days	Conc. ppm	Total Dose ; ppm-Days	Observations	Pathology
Clapp Kaye Young (1969) Abstract	Rats	ND	ND	-	1	Sub-Cutaneous	ND	Urine contains allylmercapturic acid and 3-hydroxy-propylmercapturic acid. These compounds arise by the reactions of allyl compounds with glutathiones.	None observed
Viola (1970a)	Wister Rats	M M	25 25	4	260 (5 days per wk for 12 months)	30,000 0	$1,300 \times 10^3$	Animals slightly sleepy during exposure. Gross behavior deteriorated after 10 months. 13/50 died of cardio-respiratory complications. 2/50 died of bleeding in the peritoneal cavity. No mention of skin tumors.	Most animals had pathological involvement of brain, liver, kidney, thyroid. Severe proliferation of cartilege and bone abnormalities in small metatarsal bones. Severe tissue degeneration in brain and liver and thyroid. Connective tissue invaded small arteries in feet. Enlarged, proliferating Kupfer cells in liver.
Viola (1970b)	Rats Wister 300 gm	-	90	1	1	10,000	417	Distribution of VC in tissues: Red cells had much more VC than serum--high variation VC is in urine, but major quantity is lost via lungs. VC falls rapidly in first hour in expired air, blood, urine, and brain, liver, kidney. After 3 hrs. no VC is measurable.	None observed.
Viola Pigotti Caputo (1971)	Rats Wister	M	26	4 5day/wk	260	30,000	1300×10^3		Controls showed no tumors. Almost all exptl. animals developed skin and lung tumors. Very few bone tumors; when so they were in all 4 extremities. 65%-70% of tumors were skin tumors near parotid and submaxillary glands Frequencies: SKIN 26/26 LUNGS 16/26 BONE 16/26 Lung tumors were glandular. New cartilege and subsequent ossificati- in 4 extremeties. Hard mass first seen after 10 months exposure.
		M	25	1 5day/wk	260	0	0		

SUMMARY OF TOXICOLOGICAL DATA
Animal Data

thors	Species	Sex	No.	EXPOSURE Hrs. per Day	Days	Conc. ppm	Total Dose ppm-Days	Observations	Pathology
asalaev azin ochetkov 1972) bstract	Rabbits Rats	ND ND	ND ND	ND ND	6 mos. (130 to 180 days)	12-16	ND	Changes in electrical activity of hypothalmus. Hyperadrenalirenia. Cardio-vascular function impaired. Bone resorption and osteoporosis. Theory: All symptoms are caused by hypothalmus disfunction and subsequent hormone imbalance.	

Animal Data

AUTHORS	ANIMALS			EXPOSURE				OBSERVATIONS	PATHOLOGY			
	Species	Sex	No.	Hrs/Day	Days	conc. ppm	total dose ppm-days	Survivors	Total	Liver Angiosarcomas	Zymbal Sarcomas	Nephro-Blastomas
Maltoni 1974	Rats Sprague-Dawley	M	309	4	635	10,000	$<1050 \times 10^3$	0/69	27	6	13	3
		F	268	5da/wk		6,000	$<615 \times 10^3$	0/72	31	11	5	3
						2,500	$<265 \times 10^3$	0/74	31	9	2	6
						500	$<52.9 \times 10^3$	0/67	16	7	3	3
						250	$<26.5 \times 10^3$	1/67	11	2	0	5
						50	$<5.3 \times 10^3$	3/64	0	0	0	0
						0	0	1/68	0	0	0	0
	Rats Sprague-Dawley	M	265	4	280	10,000	466×10^3	36/60	3	0	3	0
		F	280	5da/wk		6,000	280×10^3	48/60	1	0	1	0
						2,500	167×10^3	54/60	0	0	0	0
						500	23×10^3	56/60	0	0	0	0
						250	11.7×10^3	44/60	0	0	0	0
						50	2.3×10^3	50/60	0	0	0	0
						0	0	103/190	0	0	0	0
	Rats Sprague-Dawley	M	30	4	155	30,000	775×10^3	60/60	2	0	2	0
		F	30	5da/wk								
	Rats breeders	M	36	4	7	10,000	11667	28/30	0			
		F	110	(day 12-18 of preg.)		6,000	7000	28/30	0			
	off-spring					10,000	11667	30/34 (?)	1 (subcutaneous angiosarcoma)			
						6,000	7000	30/32	1 (subcutaneous antiosarcoma)			

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ENVIRONMENTAL ASPECTS OF VINYL/POLYVINYL CHLORIDE

US EPA NATIONAL ENVIRONMENTAL RESEARCH CENTER

OCTOBER 15, 1974

COMMENTS

General

1, 1 Summary

2nd par. The first important use of vinyl chloride was in the manufacture of rubber substitutes; not in the manufacture of synthetic rubber.

7th par. Analysis of vinyl chloride usually reveals trace amounts of organic impurities such as acetylene, 1, 3 butadiene, methyl chloride, and ethylene dichloride. Vinylidene(?) and vinyl acetate are introduced in the polymerization process. Polyvinyl chloride contains residual entrapped VCM in the parts per million range. The entrapped VCM concentration is dependent upon the production process and can range from nil to 1,000 to 2,000 ppm which may be liberated during storage or fabrication.

17th par. The paragraph infers that vinyl chloride is the only cause of angiosarcoma in man. The number of angiosarcoma cases in the United States has been variously estimated as 25 to 75 per year. The fifteen cases related to VCM exposure have occurred since 1961. The primary fact is that a significant number occurred in one plant in one geographical area. In the high population density

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COMMENTS

General

The report was obviously written by several groups without overall control of direction or conclusions. There is a great deal of overlap betw en the various sections.

1.1 Summary

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northeast, every case of angiosarcoma could be a community case if nearness to PVC resin is a criteria.

19th par. The conclusion in this paragraph is based on limited studies in the Louisville, Kentucky area and is not supported by the broader epidemiological survey done by Tabershaw/Cooper Associates.

1.2 Conclusions

1.

2. .....

However, cases of liver angiosarcoma have been reported among workers exposed to VCM but not directly involved in PVC production, raising the question of effects at lower levels of exposure.

This conclusion ignores the fact that angiosarcoma occurs in man for other reasons than VCM exposure. The presence of VCM in these cases is an assumption not supported by facts.

3. Observations among workers and in experimental animals indicate there is a multiple cancer risk from exposure to vinyl chloride.

The conclusion that human data exists indicating a multiple cancer risk is based on studies done in small worker populations without use of control groups. Such work lacks credence.

4.

5. The EPA studies showed one sample out of many that reached 33 ppm. In normal good analytical practice where 90% of the samples were less than 1 ppm, the existence of one sample at 33 ppm would be viewed as an accident or an error in technique. The one 33 ppm result is given weight far beyond its value in the conclusion.

6.

7. Interim methodology is available for monitoring VCM in the atmosphere, but its precision and accuracy have not been demonstrated in low VCM concentrations (<10 ppb).

8.

9.

10.

11.

12. The emissions data ..... is not sufficiently accurate to serve as a basis for the formulation of a quantitative emissions control strategy. This conclusion is very true. Only plants with continuous monitors can obtain this data.

13. The practicality and effectiveness of carbon adsorption systems, surveillance-maintenance programs, and deep stripping of the polymer remain to be demonstrated as commercially visible control techniques. This true statement also applies to ozone oxidation and incineration.

2. Introduction

1st par. ..... In the absence of appropriate premarket testing ..... appropriate premarket testing is only revealed by retrospective analyses.

4th par. .....Vinyl chloride may be disseminated on a broad scale as an unreacted monomer entrapped in finished products .....

This statement implies a hazard to finished plastic products based on no data. If all PVC resin produced contained 1,000 ppm of free VCM (which all do not), the health hazard contribution from this area would still be insignificant as compared to VCM and PVC resin plants.

4.1

4.1.1 Spectrophotometry

At lease one installation of infrared spectrometry, using the Fourier transformation, has been installed in a plant with multipoint detectors. Sensitivity of less than 1 ppm is claimed.

4.1.2

4.1.3

4.1.4 Sample collection.

4.1.5 Liquid scrubbers.

4.1.6 Solid scrubbers.

4.1.7 Sample preparation.

4. 1. 7 Environmental appraisal. 6.

5. 1

5. 2

Table

5. 2. 2 PVC Polymer Plant Emissions Data

The process data for the Firestone Tire and Rubber Company and the B. F. Goodrich Company is in error. Neither operates a solution polymerization process. Both manufacture suspension resin for solution application; i. e., lacquer-type coatings.

Union Carbide Corporation produces vinyl resins by suspension, emulsion, and solution polymerization.

5. 2. 3

5. 3. 2 Summary

In all the monitoring data, only one sample shows 33 ppm or even near it. A more scientific approach would be to discount this sample as an error. Errors must occur as frequently in EPA's laboratories as they do elsewhere.

This is substantiated by the discussion of duplicate samples which were analyzed in two different laboratores. These duplicate analyses disagreed markedly.

5.4 Estimates of Air Quality Concentrations

Estimates made by diffusion equations have not been substantiated by actual test data. This estimate is nothing more than a mathematical exercise. Union Carbide Corporation's actual monitoring has been factorially less than diffusion calculations.

5.5 Transformation, Transport, and Removal

6 Environmental Exposure and Receptor Risk

The presumption that respirable PVC dust contains measurable amounts of VCM is in error. Resin dust in the range of .3 micron to 10 microns contains no detectable VCM. Only large resin particles, 50 to 150 microns, contain VCM, and these are neither dust nor respirable.

Peak exposures to vinyl chloride in occupational situations may, at times in the past, have exceeded 1,000 ppm ..... although the highest weighted average exposures were probably in the 250-500 ppm range.

This statement is in error since it was based on the presumption that the threshold odor limit for VCM was 250 ppm. Data submitted by Union Carbide Corporation showed the threshold

odor limit was nearly 2,000 ppm; thus, the concentrations quoted could be higher by a factor of 8.

For populations residing in the vicinity of industrial sources preliminary data, described earlier, show peak exposure of 33 ppm and 24-hour samples as high as 1-2 ppm.

The statement of 33 ppm peak is based on one unsubstantiated sample; thus, again undue weight is given potentially poor data.

Table 6.1.1 Relative Importance of Vinyl Chloride Sources for the General Adult Population (mg VCM)

The correct unit is μg; not mg.

Table 6.1.2 Frequency of Liver Angiosarcoma Among Deceased Vinyl Chloride Workers

The mortality data from the Tabershaw/Cooper Associates study is conspicuous by its absence. This data has been published and subjected to critical review.

7.1.6.1 Toxicity of Polyvinyl Chloride

The free radical content and the level of residual vinyl chloride monomer of PVC resins and plastic end products could effect their toxicity, including potential for carcinogenic activity.

This observation is based on no facts. PVC contains very little, if any, free radicals. The nature of the polymerization chain termination precludes this situation. The residual monomer problem occurs only with suspension and bulk polymerized resins and is a temporary situation. PVC will not give off monomer through depolymerization; thus, the emission is limited to th amount left in the manufactured resin. Resin particles of 10 microns or less usually contain no monomer within 24 hours of manufacture.

7.1.6.2 Toxicity of Pyrolytic Products of PVC

Pyrolytic products of PVC have been well identified in a number of published studies. The presence of known carcinogens has not been confirmed. The primary products of pyrolysis are hydrogen chloride, carbon, and some light hydrocarbons.

7.3.22 The odor threshold for vinyl chloride in air is approximat ly 2,000 ppm; not 250 ppm, per Union Carbide Corporation testimony. The estimated historical exposure of workers, where odor was

used as means of estimation is 8 to 10 times that reported with peaks to 10,000 ppm.

7.3.23 The comments regarding fabricating plants do not distinguish between types of resin used and the fabricating technique. Plants based on plastisol technology generally have nil VCM concentration.

As noted in a previous comment, Union Carbide Corporation data indicates that respirable PVC dust contains no measurable amounts of monomer; thus, employee exposure via this route is negligible.

7.3.24 The questions regarding health studies are very well taken. While there are no published reports, data from control groups tend to duplicate that of the VCM exposed workers. The similarity of exposed workers and control groups is disparaged since control groups come from the same plant or area. When control groups are chosen from outside the area, then uniformity of evaluation becomes a problem.

There is a great deal of health study work to be done on a scientific basis as opposed to an emotional basis.

7.3.38 Th odor thr shold of vinyl chloride monomers

7.4 Ecology

7.5 Vinyl Chloride in Perspective

Table 7.5.1 Table 7.5.1 is confused. Polyvinyl acetate, polyvinyl alcohol, polyvinyl butyral, and polyvinyl formal have no relationship to vinyl chloride unless one is concerned about the vinyl group (C = C). If this is the case, then ethylene, propylene, styrene, acrylates, etc. should have been included.

When carcinogenic studies were undertaken, they were of insufficient exposure duration or involved too limited a number of animals to provide conclusive negative results.

Within the emotional framework of the carcinogen problem and the desire for zero cases, there are no facilities in the world large enough to hold all the animals required to provide conclusive negative results. The author's statement sounds good but it infers that the impossible is possible; i.e., prove a negative result.

8.0 Control Technology and Remedial Actions

8.1 Introduction

Controls for VCM production do not include activated carbon adsorption or ozone oxidation. The introduction implies these exist.

The discussion of emission control would be more meaningful if finite numbers were used. The citing of percentage reductions without the base number leads to misunderstanding. In repeated reference to carbon adsorption and ozone oxidation leads one to assume these are established technology. Carbon adsorption is being tested on a limited scale, and ozone oxidation is not being tested at all.

8.3.4 Solution polymerization is a proprietary process of Union Carbide Corporation that in no way resembles the emission characteristics of the suspension process or the emulsion process.

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