Interpretive Review of the Potential Adverse Effects of Chlorinated Organic Chemicals on Human Health and the Environment

- Vinyl Chloride (VCM) and Polyvinyl Chloride (PVC) -

Report of an Expert Panel

May 26, 1993

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Expert Panel Members

E. Delzell, S.D.
The University of Alabama at Birmingham
Department of Epidemiology
School of Public Health
Birmingham, Alabama

J. Doull, Ph.D., M.D.
Environmental & Occupational Health Center
University of Kansas Medical Center
Kansas City, Kansas

John Giesy, Ph.D.
Department of Fisheries & Wildlife
Michigan State University
East Lansing, Michigan

D. Mackay, Ph.D.
Department of Chemical Engineering & Applied Chemistry
University of Toronto
Toronto, Ontario

I.C. Munro, Ph.D., F.R.C.Path, Chairman
CanTox Inc.
Mississauga, Ontario

G. M. Williams, M.D.
American Health Foundation
Valhalla, New York

[1] This report was prepared, under the direction of the Expert Panel, by CanTox Inc. with supervision by Robert F. Willes, Ph.D. The Expert Panel provided direction in the preparation of the documents and critical scientific interpretation of the issues addressed in each product category document. The documents provide an interpretive review of the significance of observed past, present, and predicted future environmental concentrations of chlorinated organic chemicals to human health and the environment.

Members of the Expert Panel and Area of Their Expertise

Dr. Elizabeth Delzell, Ph.D., is Professor of Epidemiology, School of Public Health, University of Alabama, Birmingham. Dr. Delzell is an expert in the field of epidemiology and has provided critical review and analysis of the interpretation of the epidemiological and case studies of the chemicals included in the product category documents.

Dr. John Doull, Ph.D., M.D., is Professor of Pharmacology and Toxicology, and Director, Center for Environmental and Occupational Health, University of Kansas Medical Center. Dr. Doull is an expert in human toxicology, and provided critical review and analysis in the areas of mammalian toxicology, metabolism and carcinogenicity of the chemicals included in the product category documents.

Dr. John Giesy, Ph.D., is Distinguished Professor of Fisheries and Wildlife, Michigan State University in East Lansing. Dr. Giesy is an expert in aquatic toxicology, and provided critical review and analysis in the areas of aquatic and wildlife toxicology and the interpretation of natural and anthropogenic sources, environmental concentrations and environmental fate of the chemicals included in the product category documents.

Dr. Donald Mackay, Ph.D., is Professor, Department of Chemical Engineering and Applied Chemistry, and Chairman, Environmental Engineering Program, University of Toronto. Dr. Mackay is an expert in the environmental fate of organic chemicals, and provided critical review and analysis in the area of environmental chemistry and fate, and sources and environmental concentrations of the chemicals included in the product category documents.

Dr. Ian Munro, Ph.D., is President, CanTox Inc. and an expert on toxicology and health safety and highly experienced in dealing with complex regulatory issues related to product safety. Dr. Munro provided critical review and analysis of the major components considered in the safety assessment of the chlorinated chemicals and in the area of regulatory toxicology.

Dr. Gary Williams, M.D., is Director of the American Health Foundation, Valhalla, NY, and a Research Professor, Department of Pathology, New York Medical College, Valhalla, NY. Dr. Williams is an expert on chemical carcinogenicity/mutagenicity, and provided input into the critical area of biochemical aspects of toxicity and carcinogenicity of the chemicals included in the product category documents.

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PREFACE

Over the past two to three decades, concerns about chlorinated chemicals have increased and there are divergent opinions regarding how society should react to the use of these chemicals. Sound scientific information has historically been the driving force behind the identification of concerns regarding the adverse effects of chemicals in the workplace and environment. Similarly, future actions governing the production and use of chemicals by society should also be based on the best possible scientific evaluation of the consequences of their uses with respect to maintaining a viable balance between environmental quality and providing clear benefits to society. Such scientific evaluation requires an understanding of i) the potential for chlorinated organic chemicals to produce adverse effects on the ecosystem, including humans, ii) the contributions of both anthropogenic (*i.e.*, related to human activities) and natural (independent of human activities) sources of chlorinated chemicals to total concentrations versus the environment, iii) the environmental fate of the chemicals that determine the distribution and losses from the environment, and iv) the determination of the degree of anthropogenic activities that could be sustained without exceeding the assimilative capacities of the environment and the occurrence of adverse effects.

In an effort to assist continued progress in the application of sound scientific principles to the assessment of the potential adverse effects of chlorinated chemicals, a series of documents have been prepared, under the direction of an expert panel, that provide a detailed review and interpretive evaluation of the scientific information available on the historical, current and future status of chlorinated chemicals in the environment. The objective of this interpretive review was to provide an overview perspective on the potential adverse effects on the environment of chlorine and chlorinated organic chemicals for eight categories of products that involve specific chlorinated organic chemicals. The product categories identified included: chlorine, polychlorinated biphenyls, vinyl chloride/polyvinyl chloride, chlorinated organic solvents, chlorine disinfection of drinking water/waste water, incineration of chlorinated materials, bleaching wood pulp for production of paper, and the use of chlorine in the development of pesticides. For each of the first seven product categories, an interpretive review of the potential effects on human health and the environment of representative chlorinated chemicals of potential concern has been prepared. For the eighth product category, pesticides, a slightly different approach was adopted which addressed the issue of risk/benefit analysis as applied to the use of chlorine in the development of pesticides. Copies of all documents are available from the Chlorine Institute

The protocol followed in preparation of the seven product category documents has been outlined below.

- A preliminary list of chlorinated chemicals of the greatest concern and of the most relevance to each of the product categories was developed based on published quantitative analytical and hazard data. A total of 93 chlorinated chemicals were identified and were grouped by chemical class (*i.e.*, chlorinated inorganics, chlorinated alkanes, chlorinated alkenes) (see Table 1-1).

- It was beyond the scope and intention of the interpretive review to conduct a detailed assessment of the environmental and health effects of all 93 chlorinated chemicals. The

pertinent mammalian toxicity data for all 93 were reviewed and th chemicals were further classified according to their mechanisms of action (*i.e.*, genotoxic carcinogen, non-genotoxic carcinogen, mutagen, systemic toxicity) based on the most critical toxicological endpoint for which a positive effect was observed. Details of the hazard information used in the chemical selection process has been summarized in Appendix I of a document entitled "Interpretive Review of the Potential Adverse Effects of Chlorinated Organic Chemicals on Human Health and the Environment - General Introduction and Methods -".

- Based on the hazard classification, two or three representative chemicals from each chemical group, for which there were considerable hazard data in the scientific literature, were selected for detailed assessments of potential effects on the ecosystem, including humans, with respect to each product category. This approach tended to focus on the most potent compounds (*i.e.*, carcinogens); however, since not all chlorinated organic chemicals are carcinogenic, a number of chlorinated chemicals acting via mechanisms not involving carcinogenesis have also been included for detailed assessment (*i.e.*, 2,4-dichlorophenol a systemic toxicant versus 2,4,6-trichlorophenol, a liver carcinogen). The potential effect on the ecosystem of approximately 42 representative chlorinated chemicals/chemical groups from the original 93 chemicals of concern, relevant to each product category, were selected for detailed assessment (Table 1-2).

- Due to differences in species sensitivity to specific chemicals within a chemical group and the influence of abiotic and biotic environmental factors on toxicity, the potential effects of the chemicals on the environment (aquatic, terrestrial and other) were dealt with on a chemical group basis. This involved an interpretive review of the relevant toxicity data for all of the chlorinated chemicals per chemical group included in the preliminary list (see Table 1-1).

- A discussion of both natural and anthropogenic sources contributing to historical, present and future environmental concentrations, the physical-chemical properties governing their environmental fate and biological behaviour, and the environmental fate of the representative chlorinated chemicals has also been presented.

- To provide a balanced perspective of the potential for human and wildlife exposure to these compounds associated with each product category, historical and present ambient environmental concentrations or emission levels were identified for the representative chemicals on a product category basis. From a comparison of the identified environmental concentration data and the critical hazard data (*i.e.*, exposure limit or guideline), the likelihood of adverse human health or environmental effects associated with each product category was identified. Qualitative estimates of future releases to and disposition in the environment, based on best-available technologies, industry standards, and government emission policies, were used to make predictions regarding future environmental concentrations of chlorinated organic chemicals and their potential effect on human health and the environment.

- To maintain a balanced perspective of the effect of chlorinated chemicals on human and environmental health, the health benefits to society associated with the use of chlorine

use (*i.e.*, chlorine disinfection) as well as alternatives were examined and considered in the final conclusions regarding the human health and environmental effect of each product category, where information on alternatives were available.

Table 1-1 Preliminary List of Chemicals of Concern Per Product Category

CHEMICAL GROUP	Chemical	PRODUCT CATEGORY						
		Drinking Water	Waste Water	Solvents	Incineration	Pulp & Paper	PVC/VCM	PCBs
Chlorinated Inorganics								
	HCl				●		●	
	Chlorate	●						
	Chlorite	●						
Chlorinated Alkanes								
	Dichloromethane	●	●	●	●			
	Chloroform	●	●	●	●	●		
	Carbon Tetrachloride		●	●	●			
	Chloromethane			●	●			
	Bromodichloromethane	●	●	●				
	Chlorodibromomethane	●	●	●				
	Trichlorodihydroxyethane	●	●					
	Chloroethane	●	●	●				
	Dichloroethane	●	●					
	1,1-Dichloroethane			●	●			
	1,2-Dichloroethane			●	●			
	Trichloroethane		●					
	1,1,1-Trichloroethane			●				
	1,1,2-Trichloroethane			●	●			
	1,1,2,2-Tetrachloroethane			●	●			
	Bromodichloroethane			●				
	Hexachloroethane			●				
	Pentachloroethane			●				
	Dibromochloropropane	●	●					

Table 1-1 Preliminary List of Chemicals of Concern Per Product Category

CHEMICAL GROUP	Chemical	PRODUCT CATEGORY						
		Drinking Water	Waste Water	Solvents	Incineration	Pulp & Paper	PVC/VCM	PCBs
Chlorinated Alkanes (Continued)	1,2-Dichloropropane		●	●				
	1,2-Dibromo-3-chloro-propane			●				
Chlorinated Alkenes								
	Dichloroethylene		●					
	1,1-Dichloroethylene			●	●			
	1,2-Dichloroethylene (Cis)			●				
	1-2,Dichloroethylene (Trans)			●				
	Trichloroethylene		●	●	●			
	Tetrachloroethylene		●	●	●			
	1,3-Dichloropropene (Cis)			●				
	Pentachloropropene					●		
	Pentachlorobutadiene					●		
	Hexachlorobutadiene			●		●		
	Hexachlorocyclopentadiene			●				
	Hexachlorohexatriene					●		
	Vinyl Chloride			●	●		● (monomer)	
PVC								
	Polyvinyl Chloride						●	
Chlorinated Acids								
	Monochloroacetic Acid	●	●					
	Trichloroacetic Acid	●	●					

Table 1-1 Preliminary List of Chemicals of Concern Per Product Category

CHEMICAL GROUP	PRODUCT CATEGORY						
	Chemical	Drinking Water	Waste Water	Solvents	Incineration	Pulp & Paper	PVC/VCM	PCBs
Chlorinated Ketones								
	Trichloroacetone					●		
	Tetrachloroacetone					●		
	1,1-Dichloropropanone	●	●					
	1,1,1-Trichloropropanone	●	●					
	Dichlorocyclopentene-1,2-dione (various isomers)					●		
	3-Chloro-4-[dichloromethyl]-5-hydroxy-2(5H)-furanone	●	●			●		
Chlorinated Benzenes								
	Chlorobenzene		●	●				
	Dichlorobenzene		●					
	1,2-Dichlorobenzene			●	●			
	1,3-Dichlorobenzene			●				
	1,4-Dichlorobenzene			●	●			
	Trichlorobenzene		●					
	1,2,4-Trichlorobenzene			●	●			
	Pentachlorobenzene			●				
	Hexachlorobenzene			●	●			
	Dichlorotoluene		●					
	2-Chloroethylbenzene		●					

Table 1-1 Preliminary List of Chemicals of Concern Per Product Category

CHEMICAL GROUP	PRODUCT CATEGORY						
	Chemical	Drinking Water	Waste Water	Solvents	Incineration	Pulp & Paper	PVC/VCM	PCBs
Chlorinated Phenols, Catechols, Guaiacols								
	2-Chlorophenol	●	●	●				
	2,4-Dichlorophenol	●	●	●	●	●		
	2,6-Dichlorophenol					●		
	2,4,5-Trichlorophenol			●	●			
	2,4,6-Trichlorophenol	●	●	●		●		
	2,3,4,5-Tetrachlorophenol			●		●		
	2,3,4,6-Tetrachlorophenol		●	●		●		
	Pentachlorophenol		●	●	●	●		
	Tetrachlorophenol					●		
	Dichlorocatechol					●		
	Tetrachlorocatechol					●		
	Trichlorocatechol					●		
	3,4,5-Trichlorocatechol					●		
	4,5-Dichloroguaiacol					●		
	Dichloroguaiacol (other isomers)					●		
	Tetrachloroguaiacol					●		
	Trichloroguaiacols					●		
	Trichlorodihydroconiferyl Alcohol					●		
	Chlorovanillin					●		
	Trichlorovanillylalcohol					●		
	Trichloroacetosyringone					●		
	Dichloro-3,4-dihydroxy-propiophenone					●		

Table 1-1 Preliminary List of Chemicals of Concern Per Product Category

CHEMICAL GROUP	PRODUCT CATEGORY						
	Chemical	Drinking Water	Waste Water	Solvents	Incineration	Pulp & Paper	PVC/VCM	PCBs
Chlorinated Nitrogenous Compounds								
	Dichloroacetonitrile	●	●					
	Nitrochloroform	●	●					
Chlorinated Aldehydes								
	Trichloroethanal	●	●					
	Chloropropenal					●		
	Chloromethoxydibenzaldehyde					●		
	Chloralhydrate	●						
Chlorinated PCDDs, PCDFs								
	2,3,7,8-T_4CDD		●		●	●	●	
	1,2,3,7,8-P_5CDD		●		●	●	●	●
	1,2,3,4,7,8-H_6CDD		●		●	●	●	
	1,2,3,4,8,9-H_6CDD		●		●	●	●	●
	1,2,3,6,7,8-H_6CDD		●		●	●	●	●
	1,2,3,4,6,7,8-H_7CDD		●		●	●	●	
	O_8CDD		●		●	●	●	
	2,3,7,8-T_4CDF		●		●	●	●	
	2,3,4,7,8-P_5CDF		●		●	●	●	
	1,2,3,7,8-P_5CDF		●		●	●	●	
	1,2,3,4,7,8-H_6CDF		●		●	●	●	
	1,2,3,7,8,9-H_6CDF		●		●	●	●	
	1,2,3,6,7,8-H_6CDF		●		●	●	●	●
	2,3,4,6,7,8-H_6CDF		●		●	●	●	

Table 1-1 Preliminary List of Chemicals of Concern Per Product Category

CHEMICAL GROUP	Chemical	PRODUCT CATEGORY						
		Drinking Water	Waste Water	Solvents	Incineration	Pulp & Paper	PVC/VCM	PCBs
Chlorinated PCDDs, PCDFs (Continued)	1,2,3,4,6,7,8-H_7CDF		●		●	●	●	●
	1,2,3,4,7,8,9-H_7CDF		●		●	●	●	
	O_8CDF		●		●	●	●	
PCBs								
	PCBs							
Chlorinated Fatty Acids	Dichlorostearic Acid					●		
Chlorinated Resin Acids	Chlorodehydroabietic acid					●		
	Dichlorodehydroabietic acid					●		
Chlorinated Amines	3,3'-Dichlorobenzidine			●				
	4,4'-methylene-bis-(2-chloroaniline)			●				
Chlorinated Ethers	Bis(2-chloroethyl)ether			●				
Chlorinated Sulfones and Thiophenes								
	Chloro-2-thiophenic Acid					●		
	Chlorothiophenedicarboxylic Acid					●		
	1,1-Dichlorodimethylsulfone					●		
TOTAL NO. CHEMICALS	93	22	49	44	37	54	20	18

Table 1-2 Representative Priority Chemicals Assessed in Stand-Alone Documents

CHEMICAL GROUP	Chemical	PRODUCT CATEGORY							
		Chlorine	Drinking Water	Waste Water	Solvents	Incineration	Pulp & Paper	PVC/VCM	PCBs
Chlorinated Inorganics									
	Cl_2	■							
	ClO_2		■						
	HCl					■		■	
	Chlorate		■						
	Chlorite		■						
Chlorinated Alkanes[a]									
	Chloroform		■	■	■	■	■		
	Carbon Tetrachloride			■	■	■			
	Dichloromethane								
	1,1-Dichloroethane		■	■	■	■			
	1,2-Dichloroethane		■	■	■	■			
	dichloromethane	■	■	■	■				
	1,1,1-Trichloroethane				■				
Chlorinated Alkenes[a]									
	Trichloroethylene			■	■	■			
	1,1-Dichloroethylene				■	■			
	Tetrachloroethylene				■				
	Vinyl Chloride/PVC					■		■	
	Hexachlorobutadiene						■		
Chlorinated Acids[a]									
	Trichloroacetic acid		■	■					

Table 1-2 Representative Priority Chemicals Assessed in Stand-Alone Documents

CHEMICAL GROUP	Chemical	Chlorine	PRODUCT CATEGORY: Drinking Water	Waste Water	Solvents	Incineration	Pulp & Paper	PVC/VCM	PCBs
Chlorinated Ketones[a]									
	Trichloroacetone						■		
	Tetrachloroacetone						■		
	1,1-Dichloropropanone		■	■					
	1,1,1-Trichloropropanone		■	■					
	Dichlorocyclopentene-1,2-dione						■		
	3-Chloro-4-[dichloromethyl]-5-hydroxy-2(5H)-furanone		■	■			■		
Chlorinated Benzenes[a]									
	Hexachlorobenzene				■	■			
	Dichlorobenzene			■	■	■			
	1,4-Dichlorobenzene								
	1,4-dichlorobenzene			■	■				
	1,2,4-Trichlorobenzene			■	■	■			
Chlorinated Phenols, Catechols, Guaiacols[a]									
	Pentachlorophenol			■	■	■	■		
	2,4,6-Trichlorophenol		■	■	■		■		
	2,4-Dichlorophenol		■	■	■	■	■		
	Chlorocatechols[b]						■		
	Chloroguaiacols[b]						■		
Chlorinated Nitrogenous Compounds[a]									
	Dichloroacetonitrile		■	■					
	Nitrochloroform		■	■					

Table 1-2 Representative Priority Chemicals Assessed in Stand-Alone Documents

CHEMICAL GROUP	PRODUCT CATEGORY							
	Chemical	Chlorine	Drinking Water	Waste Water	Solvents	Incineration	Pulp & Paper	PVC/VCM	PCBs
Chlorinated Aldehydes[a]									
	Trichloroethanal		■	■					
	Chloralhydrate		■	■					
PCDDs/PCDFs[a,c]				■		■	■	■	
PCBs[a]									■
Chlorinated Fatty Acids[a]									
	Dichlorostearic acid						■		
Chlorinated Resin Acids[a]									
	Chlorodehydroabietic acid						■		
	Dichlorodehydroabietic acid						■		
Chlorinated Sulfones and Thiophenes									
	1,1-Dichlorodimethylsulfone						■		

[a] Environmental effects to be discussed for the group of chlorinated chemicals in the preliminary list (see Table 1-1).
[b] Human and mammalian toxicity data to be discussed for the chemical group.
[c] 2,3,7,8- substituted dioxin and furan isomers.

EXECUTIVE SUMMARY

This document focuses on the interpretation of the potential adverse effects of vinyl chloride (VCM) and polyvinyl chloride (PVC) on human health and the environment. Potential secondary effects related to pyrolysis products from VCM and PVC are addressed in the Product Category document entitled "Interpretive Review of the Potential Adverse Effects of Chlorinated Organic Chemicals on Human Health and the Environment - Incineration of Chlorinated Chemicals -". The assessment of the potential adverse effects of VCM and PVC has been based on the application of the dose-response principles that govern the actions of chemicals on biological systems as outlined in a document entitled "Interpretive Review of the Potential Adverse Effects of Chlorinated Organic Chemicals on Human Health and the Environment - Introduction and Methods -".

The overall conclusions of the interpretive review of the available information on VCM and PVC are:

i) No potential adverse effects to public health or the general environment would occur from PVC. The primary concern regarding PVC relates to occupational exposures to PVC dusts arising from the use of PVC materials in manufacturing processes.

ii) Historical (pre-1970s) concentrations of VCM in work environments of production/manufacturing facilities were excessive (in the range of 100 to 1000 ppm), and resulted in increased risks of liver angiosarcoma in workers.

iii) Although no data were identified on the concentrations of VCM in air at locations remote from production/manufacturing facilities, based on the concentrations reported near such facilities and the rapid rate of disappearance half-life of VCM in ambient air, the concentrations of VCM in air in remote locations would be expected to be infinitesimal.

iv) Following an in-depth, detailed review of the available epidemiological information on VCM, Sir Richard Doll (1988) concluded that "according to any reasonable criterion, the hazard to the general public (if there is any at all) must be negligible" from VCM exposures at locations remote from VCM production/manufacturing facilities. This conclusion is in agreement with the prediction that the concentrations of VCM in air in remote locations would be infinitesimal, and substantially less than current analytical detection limits (< 5 ppb).

v) With the exception of spills related to transportation and use, and accidental releases from point sources, the predicted risks to populations assumed to be constantly exposed to the detection limit for concentrations of VCM in air (< 5 ppb as reported in the mid-1980s within a few hundred meters of production/manufacturing facilities), would be in the range of one per million to one per 10 million.

vi) The implementation of non-emissive technologies would be expected to diminish the already undetectable concentrations of VCM in air near production/manufacturing facilities, and thereby further diminish the already infinitesimal, and unmeasurable potential risk to human health and the general environment. However, continued product stewardship is required to ensure spills

and accidental releases are controlled to ensure no adverse effects to human health or the environment occur from the use of VCM in the future.

The supporting evidence for this conclusion is based on an assessment of sources, environmental fate, hazard potential and environmental concentrations of PVC and VCM.

Physical/Chemical Properties and Environmental Fate

Polyvinyl chloride is a polymer of VCM, and is a very stable, solid material that is relatively inert chemically, environmentally and biologically. PVC does not depolymerize or degrade under natural environmental conditions. One of the historical concerns of the presence of non-polymerized VCM in PVC products has been largely addressed by modified manufacturing and production techniques. Under good manufacturing procedures, the residual concentration of VCM in modern PVC products is below analytical detection limits.

Vinyl chloride monomer (VCM) (also referred to as chloroethene, chloroethylene or monochloroethylene) is a molecule of two carbon atoms joined by an unsaturated bond and containing three hydrogen atoms and one chlorine atom. VCM has a high vapor pressure and is slightly soluble in water, consequently volatilization into the atmosphere is the major transport process in the environment. VCM is reactive, and readily polymerizes in the presence of oxygen, sunlight or heat to form PVC. Vinyl chloride monomer rapidly degrades in the troposphere via photochemical oxidation. As indicated by the low log K_{ow} of 1.38, vinyl chloride does not adsorb to organic carbon of soils/sediments or accumulate in biological tissues. Certain strains of microorganisms (*e.g., Mycobacterium*) can use vinyl chloride as a carbon and energy source under aerobic conditions. Biological degradation of VCM to CO_2 can occur under both aerobic and anaerobic conditions.

Hazard Potential of VCM

As with other chemicals, the potential for adverse effects of VCM depends on the concentrations that occur in target tissues within the body where adverse effects develop. These tissue concentrations depend on the bioavailability of the chemical from various environmental media through different routes of exposure.

At room temperature, vinyl chloride is a gas. As such, inhalation is the most significant route of exposure in the environment and in occupational settings. Vinyl chloride is readily and rapidly absorbed by the lung and readily metabolized to the reactive epoxide intermediate, chloroethylene oxide, which can rearrange spontaneously to chloroacetaldehyde, then undergo further metabolism. VCM does not accumulate in tissues.

Vinyl chloride is not a potent acute toxic agent, and acute lethality is not observed until air concentrations reach 113,000 to 230,000 ppm (294 to 595 g/m^3). At these high exposures VCM acts as a narcotic or anaesthetic agent. In addition, at acutely toxic doses, tissue damage to lung, liver and kidneys has been observed. Following repeated, non-lethal exposures, the principal target organ for VCM is the liver. VCM was not found to be teratogenic in a number f laboratory studies on mammalians.

Evidence of carcinogenicity in animals is conclusive based on positive data from numerous laboratory studies on animals. Both IARC and the U.S. EPA have concluded that there is sufficient evidence for vinyl chloride carcinogenicity in humans based upon the epidemiological data on workers exposed to high concentrations between the 1940s and late 1960s. Vinyl chloride exposure has been associated with the development of a specific cancer (angiosarcoma) of the liver. There is disagreement in the reported literature regarding the potential for VCM to produce other types of cancer; however, there of some evidence for such concerns among persons with extreme exposures such as those that occurred historically in occupational settings.

The results of *in vitro* mutagenicity studies and observations of chromosomal aberrations in peripheral blood lymphocytes in workers indicate a DNA-reactive mechanism for the mutagenicity/carcinogenicity of VCM. Vinyl chloride has also been shown to be activated, via P450 enzyme systems, to a reactive epoxide intermediate that is believed to result in alkylation of DNA.

Sources and Environmental Concentrations

The majority of VCM is produced for use in the production of vinyl chloride homopolymer and copolymer resins. Vinyl chloride is also used to a lesser extent as a component in the synthesis of methyl chloroform and as a co-monomer with vinylidene chloride to produce resins. A former use of vinyl chloride was as a propellant in aerosol cans and as a refrigerant. Polyvinyl chloride resins manufactured from VCM are used in the manufacture of a variety of industrial and commercial products ranging from building materials to household and medical items.

Undefined quantities of VCM can be produced from bio- and abiotic transformation of chlorinated solvents such as 1,1,1-trichloroethane and 1,1-dichloroethane. 1,1,1-Trichloroethane and 1,1-dichloroethane both have a number of anthropogenic and natural sources. The natural sources of these VCM precursors suggest that there may be sources of VCM produced by natural processes independent of human activities, although such sources have not been unequivocally identified to date.

The primary source of VCM in the environment is from emissions and effluents from vinyl chloride and polyvinyl chloride production and manufacturing facilities. Such releases rapidly volatilize into the atmosphere. Since 1979, VCM emissions from such production facilities have been regulated in both Canada and the United States. Prior to 1975, it was estimated that PVC plants released 22.7 million kg of PVC and 110 million kg/year of VCM into the environment in the United States. Implementation of regulatory standards have substantially reduced total environmental releases of VCM and PVC, and currently the major sources are from accidental releases and spills.

The concentrations of VCM in air are greatest near industrial facilities involved in its production and use in various manufacturing processes. Average concentrations of VCM in air in the late-1970s were 44 $\mu g/m^3$ near production facilities for Houston, Texas, and 10 to 40 $\mu g/m^3$ near facilities in England. Air concentrations near production facilities were generally below analytical detection limits ($< 13\ \mu g/m^3$ or 5 ppb) by the mid-1980s. In the work environment, air concentrations of VCM have decreased over the years with the reduction of emissions through improved operating technologies. Workplace concentrations in the Netherlands

decreased from approximately 1000 ppm in 1945-1955 to 5 ppm after 1975 (Barnes, 1980), and data from the late 1980s to the present indicate workplace air concentrations generally <0.1 ppm with occasional values near 1 ppm in specific production/handling areas. Since production and manufacturing facilities are major sources of VCM, decreases in workplace concentrations would be expected to coincide with decreases in environmental releases. This relationship is supported by the declining environmental concentrations of VCM reported near production and manufacturing facilities observed between the 1970s and early 1980s.

Potential Significance of Environmental Concentrations of VCM

The available information on the physical/chemical properties, environmental fate characteristics and sources of VCM indicate that the major environmental concerns for VCM come from exposures of production and manufacturing workers and possibly populations living near such facilities. There would be little opportunity for exposures, and therefore risks of adverse effects, to the general public, or aquatic and terrestrial wildlife from VCM at locations distant from production and manufacturing facilities. As outlined above, the air concentrations near such facilities (within a few hundred meters) were historically in the range of 10 - 40 ppb in the mid-1970s, and had decreased to values below detection limits (< 13 $\mu g/m^3$ or 5 ppb) by the mid-1980s. Based on current concentrations of VCM in air in the work environment (generally in the range of 0.1 to 0.2 ppm), the concentrations near facilities would be expected to be substantially less than analytical detection limits at the present time, and in the future.

The characterization of the potential health risks that could potentially result from exposures to such concentrations of VCM in air requires the comparison of resulting levels of exposure against a cancer potency estimate. The U.S. EPA has, over the years, proposed cancer potency slope values for VCM of 0.0174, 0.0295 and 2.3 $(mg/kg\ body\ weight\ per\ day)^{-1}$, based on lung and liver tumors, respectively, following inhalation exposure to up to 30,000 ppm VCM and oral exposure to 0-17 mg/kg body weight/day (5 days/week) in laboratory rats. These cancer potency slopes translate into RsD (Risk Specific Dose) values of 0.575, 0.339 and 0.00435 $\mu g/kg$ body weight/day at a lifetime risk of one per 100,000, a range of 132-fold, based on available laboratory information and the EPA risk assessment approach.

Cancer potency factors estimated from epidemiological studies of workers exposed to VCM in the 1940s, 1950s and 1960s, range from 0.00024 to 0.000024 $(mg/kg\ body\ weight/day)^{-1}$. These estimates assume exposures to 100 to 1000 ppm VCM resulted in a mortality incidence due to liver cancer of 2 per 100. The cancer potency estimates derived from the epidemiological data would translate into RsD values of approximately 42 to 420 $\mu g/kg$ body weight/day at a lifetime risk of one per 100,000. These exposure limits are starkly different from the greatest potency value proposed by EPA, and indicate that VCM is less potent by some 9500- to 95000-fold. Such large differences in estimates of cancer potency, using different data and approaches, result in equivalent differences in the risk estimates, and therefore, in the interpretation of the potential significance of the environmental concentrations of VCM near production/manufacturing facilities.

Risk estimates based on the EPA values range from approximately 15 to 7700 per 100,000 for the air concentrations of VCM near production facilities in the mid-1970s, and from 7.4 to 980 per 100,000 for the mid-1980s air concentrations of VCM near production facilities. Risk

estimates based on the epidemiological data range from 0.08 to 0.2 per 100,000 for the mid-1970s air concentrations, and from 0.01 to 0.1 for the mid-1980s air concentrations.

Based on a critical evaluation of the available epidemiological evidence available from workers exposed to VCM between the early 1940s and the 1960s, Doll (1988) concluded that potential risks from VCM to the "general public (if there is any at all) must be negligible". This conclusion is in agreement with the risk assessment summarized above using cancer potency estimates based on epidemiological data. Based on the environmental fate of VCM, the potential health risks to the general public in regions remote from VCM production and manufacturing facilities would be even more negligible, and certainly unmeasurable using conventional epidemiological study approaches. The maintenance of procedures for non-emissive uses of VCM and strict attention to operations to avoid accidental releases are needed to ensure that the current status of no adverse effects on human health and the environment is maintained. In the future, improved production and manufacturing control technologies and attention to accident prevention, in keeping with policies of progressive product stewardship, will continue to reduc emissions of VCM from production and manufacturing facilities, thereby further reducing the already negligible and unmeasurable risks predicted from current environmental concentrations of VCM near production and manufacturing facilities.

CHAPTER 1 INTRODUCTION

1.1 Introducti n

Polyvinyl chloride (PVC) is a rigid "plastic" polymer of vinyl chloride (VCM) and is widely used in the manufacture of a wide range of industrial and commercial products. PVC products are widely used as building materials, furnishings, plumbing materials, appliances and medical items.

PVC is physically, chemically and biologically inert; however, VCM is a reactive chemical. Although short-term exposures to VCM, even at high ppm concentrations, are without apparent toxic effects, evidence of increased liver cancers in exposed workers raised concerns regarding potential human health effects associated with VCM exposures. This document presents an interpretive evaluation of potential effects of PVC and VCM through an assessment of i) potential exposures through an analysis of sources, environmental fate characteristics and concentrations in various environmental media through which exposures can occur, ii) an analysis of the potential hazards from PVC and VCM, and iii) the characterization of potential risks to various biological systems by the comparisons between their potential levels of exposure from environmental media and the hazard potential associated with VCM and PVC. The potential concerns regarding pyrolysis products from PVC and VCM are addressed in a separate document from the Chlorine Institute entitled The Potential Adverse Effects on Human Health and the Environment from the Incineration of Chlorinated Chemicals.

CHAPTER 2 PROPERTIES, SOURCES AND ENVIRONMENTAL FATE OF VINYL CHLORIDE AND POLYVINYLCHLORIDE

2.1 Sources and Environmental Fate

2.1.1 Anthropogenic Sources

Uses

Polyvinyl chloride resins produced from VCM are used in the manufacture of a variety of products such as plastic pipes and conduit, floor covering, windows, siding, upholstery, garden hoses, appliances, gramophone records, wire and cable insulation, bottle-cap liners and gaskets, seat covers, plasticized film and automotive floor mats (IARC, 1979). Vinyl chloride-vinyl acetate copolymers are used in the manufacture of vinyl asbestos flooring tiles, gramophone records, coating resins and for sheet extrusion and injection molding. Vinylidene chloride-vinyl chloride copolymers are approved by the U.S. Food and Drug Administration (FDA) for use in food packaging products (*e.g.*, food wrap, shrink film, bottles), tubing used in the dairy industry and various types of tubing and bags used in medical applications (Vinyl Institute, 1993, personal communication). The copolymers also are used as coatings or liners for other polymer films, for plastics, paper, paperboard, cassette tapes, ship and railroad tanks, fuel storage tanks, tubes, rods and pipes. In addition, they are used in fibers, cements, laminations, colostomy bags, and as binders for paints and non-woven fabric (Wessling and Edwards, 1971; Roth, 1976; IARC, 1979). The principal products manufactured from VCM in the USA include PVC homopolymer and copolymer resins. Smaller quantities are used as a component in synthesis of methyl chloroform (1,1,1-trichloroethane) and as a co-monomer with vinylidene chloride to produce resins (IARC, 1979). The production of methyl chloroform is being phased out in accordance with the Montreal Protocol because of its potential interactions with stratospheric ozone. VCM also was used as a propellant in aerosol cans and as a refrigerant (Sax, 1986), although these uses have been discontinued and are only of historical interest.

VCM Emissions

The major anthropogenetic sources of VCM include fugitive emissions during the production of VCM and the manufacture of various products from VCM. Most of the fugitive emissions from these processes are vapors released into the air. As indicated by its environmental fate characteristics, fugitive releases into aqueous media would be rapidly volatilized to the atmosphere. Releases of VCM from various facilities have been documented. The estimated releases of VCM to the atmosphere from PVC plants, prior to 1975, was 110 million kg per year in the U.S. (EPA, 1975a). An estimated 22.7 million kg of PVC had been released into the environment from man-made sources before 1975 (EPA, 1974).

In 1981, following the implementation of regulations to control VCM emissions in Canada, a total of 41 emission incidents (*e.g.*, where emission limit of 25 mg/m^3 or 10 ppm were exceeded) occurred in Quebec, Ontario and Alberta, resulting in an estimated release of 46 tons of VCM. By 1986, the number of incidents of exceedance of the emission limit were reduced to nine and the estimated releases reduced to nine tons of VCM (Morcos, 1988).

Microbial or chemical transformation of chlorinated solvents to VCM, leaching of residual VCM monomer from polyvinyl chloride, and the possibility of degradation or depolymerization of polyvinyl chloride are considered as possible sources of VCM in ground water and landfills.

VCM From Transformation Reactions

Tetrachloroethene, trichloroethene (Parsons *et al.*, 1984; 1985; Kleopfer *et al.*, 1985; Barrio-Lage *et al.*, 1986) and 1,1,1-trichloroethane (Kleopfer *et al.*, 1985; Barrio-Lage *et al.*, 1986; Molton *et al.*, 1987) can be transformed to VCM, cis- and trans-1,2-dichloroethylene by micro-organisms in muck obtained from an aquifer recharge basin.

In addition, chemical or abiotic transformations of chlorinated solvents, although slower than biotic transformation, may result in VCM production in ground water environments. Abiotic transformations are influenced by the number and type of halogen substitution. As the halogen number increases, the relative rate of reduction increases (Vogel *et al.*, 1987). Chemical transformation of 1,1,1-trichloroethane to 1,1-dichloroethene, then to VCM, has been documented; however, depending on the environment, microbial flora, and organic content, other routes may be favored (*e.g.*, the transformation of 1,1,1-trichloroethane to 1,1-dichloroethane) (Vogel *et al.*, 1987). Abiotic transformations of trichloroethane to VCM are hindered by thermodynamic factors and activation energy barriers (Wolf *et al.*, 1987); therefore, biological, chemical or thermal catalytic effects are required to overcome the barriers. Thus, the contribution of abiotic transformation of chlorinated solvents is small compared to biotransformation (Vinyl Institute, 1990).

VCM From Residual Monomer in PVC

Prior to 1975 polyvinyl chloride contained much greater concentrations of residual monomer, thus, PVC waste sludges from old material may have contributed to initial VCM levels in landfills. However, the contribution of this source to total VCM releases to the atmosphere, water and soils is probably minor (Molton *et al.*, 1987).

The concentrations of VCM observed in landfills are not the result of degradation or depolymerization of polyvinyl chloride. The majority of the sources of VCM observed in landfills is related to the land disposal of PVC production sludges (a procedure no longer practiced), and the crushing or corrosion of cans where VCM was used as a propellant (such uses were banned in 1974) (Vinyl Institute, 1990). Temperatures typical of combustion processes are necessary to produce minor amounts of VCM from PVC, therefore, thermal degradation of PVC in landfills is not a significant source of VCM. Following PVC pyrolysis in air at 350 °C, a maximum of 35 ppm of VCM was detected, while a maximum of only 6 ppm was detected following pyrolysis of PVC at 500°C in helium (Molton *et al.*, 1987). Photolytic and degradation of PVC through high energy processes such as combustion, are also improbable sources because of the soil cover and the lack of high energy sources in landfills. PVC is also resistant to biological degradation (Vinyl Institute, 1990) and is not known to depolymerize under even severe conditions (Kirk-Othmer, 1983).

Potential Releases in Remote Locations

From the assessment of the environmental fate of VCM, it can be concluded that VCM is rapidly eliminated from the atmosphere through various photochemical oxidation processes, and that it would not accumulate in biological systems. The rapid destruction of VCM emitted into the environment would preclude the possibility of significant environmental concentrations

occurring at locations remote from its release. Concentrations of VCM in air within a kilometer f production facilities in about 1975 were approximately 10 to 40 ppb (EPA, 1975b; Baxter *et al.*, 1977). These concentrations are about 10,000-fold less than those considered an occupational hazard (Doll, 1988). Therefore, any potential adverse effects from VCM would be confined primarily to occupational settings, and would not be observed in remote locations.

2.1.2 Natural Sources

Although natural sources of some 1500 halogenated organic chemicals have been identified, mostly in the last decade (see Introduction and Methods document for details), the evidence for natural sources of vinyl chloride are, at present, indirect. Vinyl chloride derivatives have been identified as natural products of two strains of blue-green algae (*Schizothrix calcicola* and *Oscillatoria nigroviridis*) (Gribble, 1992), although these observations do not necessarily mean that these algae produce free VCM. However, tetrachloroethylene, trichloroethylene (Parsons *et al.*, 1984; 1985; Kleopfer *et al.*, 1985; Barrio-Lage *et al.*, 1986) and 1,1,1-trichloroethane (Kleopfer *et al.*, 1985; Barrio-Lage *et al.*, 1986; Molton *et al.*, 1987) are produced by various species of algae. Since these chlorinated alkanes and alkenes can be transformed to VCM by both biological and abiotic processes (Vogel *et al.*, 1987; Wolf *et al.*, 1987), the production of VCM from natural sources of these chlorinated alkanes and alkenes may also provide a natural source of VCM to the environment. However, no information is available on the quantities of the various chlorinated alkanes and alkenes produced by natural processes, therefore estimates of the potential natural production rates of VCM cannot be obtained.

2.2 Environmental Fate

2.2.1 Physical-chemical Properties

The physical/chemical properties of VCM and PVC are different (Table 2-1). VCM has a high vapor pressure and low K_{ow} value. PVC, on the other hand, is an inert, highly stable solid under a wide range of environmental conditions; however, because PVC is a polymer of variable numbers of vinyl chloride units, no overall physical/chemical properties typical to the whole class of materials can be determined. Depending on the polymerization process, some residual vinyl chloride monomer remains after the polymerization process; however, the use of best-available-technology involving proper temperature and pressure treatment in the final stages of manufacturing reduce the residual monomer concentrations to 1 ppm or less.

Table 2-1 Physical/Chemical Properties

Chemical Name	Molecular Weight (g/mol)[a]	Vapor Pressure (Pa)	Solubility (mg/L)	Log K_{ow}
Vinyl Chloride	62.5	354637.5[b]	2500[c]	1.38

[a] -from Merck, 1989.
[b] -from Verschueren, 1983.
[c] -from Torkelson and Rowe, 1981.

2.2.2 Environmental Fate

PVC is a stable polymer that remains a solid and does not degrade or migrate under normal environmental conditions. The environmental fate of degradation products formed during pyrolysis of PVC, and products of incomplete combustion are discussed in the Produce Category document entitled "Interpretive Review of the Potential Adverse Effects on Human Health and the Environment from Chlorinated Organic Chemicals - Incineration of Chlorinated Organic Products-".

Air

The rate of exchange of gaseous VCM between water and air is twice that of oxygen, thus indicating that volatilization is the major process in the environmental disposition of VCM (Hill *et al.*, 1976). The vapor density of VCM is higher than the vapor density of air, 2.2 versus 1.0 (Anon., 1972), thus vapors of VCM tend to remain near the ground (Sax, 1986).

In the environment, polymerization of VCM occurs in the presence of air, oxygen, sunlight or heat (Sax, 1986). In the troposphere, VCM undergoes photochemical oxidation with hydroxyl radicals to form hydrogen chloride or formyl chloride. Formyl chloride undergoes further reactions to form carbon monoxide and hydrogen chloride. Since these reactions are extremely rapid, the degradation half-life of VCM in the troposphere is less than one day (EPA, 1975c; EPA, 1979).

Water/Sediment

Sorption of significant amounts of VCM by sediments would occur only upon continuous input of VCM at concentrations near the solubility limit in water to aquatic systems (Hill *et al.*, 1976). The adsorption of VCM to particulate matter is considered insignificant as indicated by the same rates of loss from distilled water, river water and industrial effluents (EPA, 1974). The reported log octanol/water partition coefficient (K_{ow}) of VCM ranged from 0.60 (Radding *et al.*, 1977) to 1.78 (Mackay *et al.*, 1992), thus, adsorption to organic carbon and accumulation in lipid tissues of aquatic biota would not occur.

VCM is slightly soluble in water; however, due to its high vapor pressure, VCM entering aquatic systems would be rapidly lost to the atmosphere through volatilization (Sax, 1986; Vinyl Institute, 1990). The volatilization half-life of VCM from surface waters ranges from several minutes to a few hours depending on water turbulence (Dilling *et al.*, 1975; Hill *et al.*, 1976; EPA, 1979). In groundwater, where volatilization cannot occur, VCM may be slowly hydrolyzed with a half-life of less than ten years (Hill *et al.*, 1976; EPA, 1979; Smith and Dragun, 1984). Reaction products may include chlorinated alcohols and/or carboxylic acids (Smith and Dragun, 1984).

Direct phototransformation of VCM in surface waters would not be expected, since VCM absorbs shorter wavelengths of light than are present in the sunlight radiation spectra at the earth's surface (< 285 nm) (Hill *et al.*, 1976; EPA, 1979). However, indirect photolysis may be a factor in the transformation of VCM. Hill *et al.* (1976) demonstrated that irradiation with ultraviolet light transforms VCM, via energy transfer, when acetone or hydrogen peroxide are

present. In such reactions, acetone acts as a high energy triplet sensitizer and hydrogen peroxide as a free radical source. Oxidation of VCM in natural waters was not considered to be a significant reaction because of low temperatures and oxygen concentrations (Hill *et al.*, 1976).

There are limited data concerning the biotransformation of VCM. Lu *et al.* (1977) reported that the high volatility of VCM prevented significant transformation in a model ecosystem. Mineralization of VCM to carbon dioxide may be possible under anaerobic conditions; however, further study is required for confirmation (Vogel and McCarty, 1985). VCM has been considered to be resistant to microbial transformation (Hill *et al.*, 1976); however, more recent data shows that a strain of *Mycobacterium* can use VCM as a carbon and energy source in aerobic environments (Hartman *et al.*, 1985). *Mycobacterium* were able to metabolize 70% of the carbon present as VCM to carbon dioxide and hydrochloric acid. In soil-groundwater systems reductive dechlorination under anaerobic conditions is the predominant mechanism for the degradation of many volatile chlorinated hydrocarbons, and the production of ethylene from VCM has been hypothesized to occur through this mechanism (Smith and Dragun, 1984). The degradation of 90% of VCM by microorganisms in a shallow aquifer, with about 50% mineralization to carbon dioxide over a 106 day period has been demonstrated using ^{14}C-VCM (Davis and Carpenter, 1990).

Soil

There is a paucity of information concerning the fate of VCM in soil. However, it is expected that VCM present in superficial soils would rapidly volatilize to the atmosphere. Sorption of VCM to sediment or soil from aqueous environments is not expected to be a very important transport process (EPA, 1979). As described in the previous section, biotransformation of VCM may occur in groundwater; thus, it is probable that under proper conditions biotransformation would also occur in soils.

Environmental Fate Fugacity Modelling

Fugacity modelling of chemicals in the environment provides predictions of the partitioning, movement and behaviour of chemicals within different environmental media based on the specific physical properties of chemicals. Level I fugacity modelling predicts the distribution of chemicals to air, water, soil, bottom sediment, fish and suspended sediment given a steady-state situation where no removal of the chemical occurs by any chemical or physical processes. Level II fugacity modelling provides predictions of the rates of loss of chemicals from various compartments by reactive or advective means, again, under steady-state conditions. Level III fugacity modelling provides predictions of the rates at which a particular chemical would move between the various environmental compartments (Mackay *et al.*, 1992).

Vinyl Chloride

Level I Fugacity modelling was performed for VCM using physical and chemical properties (Table 2-2). The results are displayed graphically (Figure 2-1).

Table 2-2 Physical/Chemical Properties of Vinyl Chloride

Temperature °C	25	Fish-water partition coefficient	1.15144
M lecular mass g/mol	62.5	Air-water partition coefficient	3.576678
Vapor pressure Pa	354637.5	Soil-water partition coefficient	0.2950564
Solubility g/m³	2500	Sedt-water partition coefficient	0.590113
Solubility mol/m³	40	Susp sedt-water partition coefficient	0.590113
Henry's Law constant Pam³/mol	8865.938		
Log octanol-water partition coefficient	1.38	Amount of chemical moles	1000
Octanol-water partition coefficient	23.98833	Fugacity Pa	4.130013E-4
Organic C-water partition coefficient	9.835216	Total of VZ products	2421300

The results of the fugacity modelling indicate that virtually all VCM will partition towards the air with small amounts distributing to the other compartments. This partitioning is consistent with the vapor pressure of VCM.

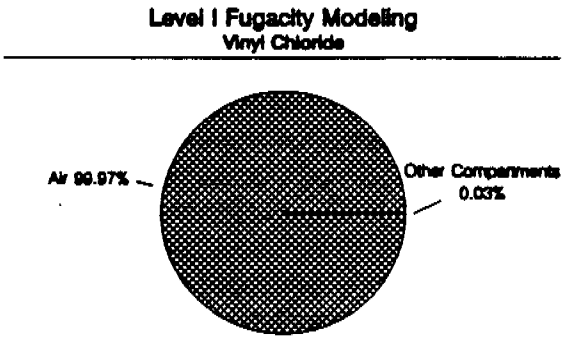

Figure 2-1

2.3 Vinyl Chloride Regulations

2.3.1 Regulations of VCM in Air

2.3.1.1 Concentrations of VCM in Emissions and Ambient Air

Regulation of emissions of VCM from manufacturing plants in the United States, effective as of July 1, 1979, requires that VCM concentrations in air emissions remain less than 25 mg/m³ (10 ppm) by volume or total releases remain less than 2 kg/day, which ever is greater (Gendron, 1981). According to IARC (1979), the EPA (1977) proposed to reduce the air emission guideline to 13 mg/m³ (5 ppm). The Federal Republic of Germany has an emission standard of 3 kg VCM/hour/source (150 mg/m³ at the source) (Thomas, 1977).

In Canada there are regulations regarding ambient air concentrations and emissions. The Ontario Ministry of the Environment (1991) guideline value for annual average VCM concentrations in ambient air is 0.2 μg/m³ based on the estimated exposure limit for the potential development of cancer at a risk level of one per 100,000. Elsewhere in Canada, the Federal Vinyl Chloride National Emission Standards Regulations (SOR/79-299) and the Vinyl Chloride Release

Regulations (SOR/90-25) stipulate that air VCM concentrations in any process vent must not exceed 25 mg/m^3 (10 ppm) (by volume, measured dry and undiluted), or two kg/day VCM released into the ambient air. For polyvinyl chloride plants, the air concentrations in any process vent must not exceed ten ppm VCM. Regulations of emissions specific to the manufacture of certain resins are also included.

The current OSHA workplace standard in the U.S. is 1 ppm (8 hour TWA) with a 5 ppm short term exposure limit (STEL).

No information concerning the environmental concentrations or emission regulatory guidelines or criteria for polyvinyl chloride was identified.

2.3.1.2 Regulations of VCM in Water

The U.S. drinking water criteria proposed by the EPA (1991) for VCM in water for human consumption was 2 μg/L. This value was based on estimated exposure limits for potential cancer in humans at a risk level of 10^{-6}. This criteria level was unchanged from that developed for water consumption by the EPA in 1980 (EPA, 1986). EPA (1986) also reported a Maximum Contaminant Level (MCL) of 925 μg/L for VCM in water. The quality standard specification used for VCM in ground water in New York State is 5.0 μg/L (New York State Department of Environmental Conservation, 1986).

2.3.1.3 Soil

No information was identified on soil or sediment quality guidelines or criteria for VCM. Since the environmental fate characteristics of VCM indicate that air is its major environmental medium, soil would not be expected to be an important environmental compartment for VCM.

CHAPTER 3 POTENTIAL ENVIRONMENTAL HAZARDS AND HEALTH SIGNIFICANCE OF ENVIRONMENTAL CONCENTRATIONS OF VCM

3.1 Introduction

The methods for characterizing the risks due to exposure to involved estimating potential human exposures to VCM from various environmental sources, and comparing these exposures to exposure limits that are considered protective of human health. The fundamental principles underlying these methods are discussed in detail in a document entitled "Interpretive Review of the Potential Adverse Effects of Chlorinated Organic Chemicals on Human Health and the Environment - General Introduction and Methods -". Therefore, Chapter 3 summarizes i) the information available on the concentrations of VCM in various environmental media, ii) the toxicological/epidemiological information available on the potential health hazards that could result from exposures to VCM, iii) the derivation of exposure limits for VCM that would be protective of human health, and iv) the comparison between the estimated exposures through various environmental media and the exposure limit to characterize potential human health risks to VCM. In addition, the potential adverse effects from ambient sources of VCM on aquatic and terrestrial wildlife are assessed and discussed.

3.2 Environmental Concentrations

The concentrations of VCM in the environment are determined by the types of environmental releases that occur during production and manufacturing processes. In 1988, an estimated total of approximately 2 million pounds of VCM was either released or transferred from production facilities in the U.S. Approximately 99% was released in point source or non-point source air emissions, 0.6% into surface waters and 0.2% to land (EPA, 1992). Only 1.4% of the vinyl chloride released is transferred to a waste treatment facility. This information indicates that the environmental concentrations of vinyl chloride would be highest in air near production and manufacturing facilities. Therefore, the following discussion of environmental concentrations of VCM focuses on air, and is divided into the work place and immediate environment near production/manufacturing facilities, and regions distant (remote) from such facilities.

3.2.1 VCM Concentrations Associated With Production/Manufacturing Facilities

Concentrations in the Indoor Work Environment

Standards for the concentrations of VCM in the work environment were presented in Section 2.3.1. Generally, concentrations of VCM in the workplace prior to the 1960s were greater than 100 ppm, decreased to values less than 100 ppm between the 1960s and mid-1970s, then decreased to an upper limit of 5 ppm (8 hour, time-weighted-average (TWA)) by 1975 (Doll, 1988; ACGIH, 1991). The current OSHA workplace standard in the U.S. is 1 ppm (8 hour TWA) with a 5 ppm short-term exposure limit (STEL). Due to the implementation of occupational health standards, the concentrations of VCM in the work environment in the Netherlands decreased from approximately 2600 mg/m^3 (1000 ppm) in 1945-1955 to approximately 12 mg/m^3 (5 ppm) after 1975 (Barnes, 1980).

In 1988, the concentrations of VCM (8 hour TWA based on individual personnel monitoring) in the work environment ranged from approximately <0.25 to 10.5 mg/m^3 (<0.1 to 4.11 ppm) in four PVC resin production facilities in the U.S.A. Reactor operators, loading personnel and laboratory technicians showed the greatest potential exposures, with 8 hour. TWA air

concentrations ranging from 0.5 to 11 mg/m^3 (0.2 to 4.11 ppm); these air concentrations had decreased to 0.5 to 2 mg/m^3 (0.2 to 0.77 ppm) in 1992. In 1990, one facility reported 8 hour. TWA concentrations in air for instrument technicians and process operators of 35 and 26.5 mg/m^3 (13.5 and 10.34 ppm), respectively. By 1992 (January to September data only), the work-place concentrations in these facilities had decreased to a range of approximately <0.25 to 2 mg/m^3 (<0.1 to 0.77 ppm). These data represent the greatest concentrations of VCM in air reported for the four facilities over the 5 year period, 1988 through 1992 (Vinyl Institute, personal communication, 1992).

Concentrations Near Production/Manufacturing Facilities

Localized releases of VCM to the natural environment occurs around production and manufacturing facilities, therefore, the concentrations of VCM are highest near such facilities. The decreases in concentrations of VCM in the work environment discussed in above would also be indicative of decreases in environmental releases from production/manufacturing facilities. However, no generalized information on this point was identified since the focus on measuring air concentrations of VCM has been on various "hot spots".

Vinyl chloride has been measured in air around suspected "hot spots" in areas near production and manufacturing facilities the United States. Prior to the implementation of VCM emission regulations in 1978, the average air concentrations of VCM at production facilities in the United States was 44 μg/m^3 (17 ppb) (IARC, 1979). In Houston, Texas where large quantities of VCM are produced, air concentrations ranged from 8 μg/m^3 (3.1 ppb) to peak values of 3,200 μg/m^3 (1,200 ppb) (Gordon and Meeks, 1977). In Long Beach, California, ambient air concentrations of VCM near two VCM plants ranged from 260 to 8,800 μg/m^3 (100 to 3,400 ppb), and these facilities were estimated to have released 12.3 kg of VCM/day in waste water effluent (National Field Investigations Center, 1974). However, within approximately one kilometer of VCM production/manufacturing facilities, reported air concentrations of VCM ranged from approximately 26 to 100 μg/m^3 (10 to 40 ppb) (EPA, 1975b; Baxter *et al.*, 1977). More recent information based on sampling near production/manufacturing facilities since standards for the work environment were reduced to about 13,000 μg/m^3 (5 ppm) in 1975, showed that air concentrations of VCM were near the analytical detection limit (about 13 μg/m^3 or 5 ppb) in three of five British plants. For two other facilities, the VCM air concentrations were approximately 50 μg/m^3 (20 ppb) 100 m outside the facility boundary, and 225 μg/m^3 (88 ppb) just inside the boundary fence (Turner *et al.*, 1984).

Vinyl chloride also has been measured in both ground water and drinking water in the United States. The greatest concentration of VCM measured in U.S. drinking water was 10 μg/L near a production facility (Safe Drinking Water Committee, 1977; IARC, 1979). Vinyl chloride monomer has also been reported in ground water in the U.S.A. Measurable levels in California wells averaged 20 μg/L and were as high as 23 μg/L (Kizer, 1986). In the Los Angeles area, ground waters contained less than 1 μg/L of VCM (Baird *et al.*, 1983), while in non-specified areas of Nebraska and California ground water concentrations ranged from 0.75 to 23 μg/L (Goodenkauf and Atkinson, 1986; CSDHS, 1990).

3.2.2 VCM Concentrations Remote from Production and Manufacturing Facilities

No information was identified on the concentrations of VCM in air in locations remote from industrial activities. However, it would be expected that the VCM concentrations in such locations that are derived from human activities would be below analytical detection limits, based on: i) the continuing decline in VCM concentrations in the workplace (Table 2-2), ii) the low concentrations measured near production/manufacturing facilities using VCM (EPA, 1975b; Baxter *et al.*, 1977; Turner *et al.*, 1984), and iii) the rapid vaporization of VCM and subsequent destruction in the atmosphere.

3.3 Hazard Assessment

3.3.1 Polyvinyl Chloride

PVC has several synonyms, PVC has also been referred to as chloroethene homopolymer, chloroethylene polymer, vinyl chloride homopolymer, and vinyl chloride polymer.

There are limited data regarding the toxicology of PVC, with the majority of studies focusing on the pulmonary effects of this polymer. No data on the embryotoxicity, teratogenicity, metabolism, or mutagenicity of this compound were identified by IARC (1979) or subsequent searches of the available literature.

3.3.1.1 Bioavailability, Metabolic Conversion (Pharmacokinetics), and Bioaccumulation

The available data indicate that following a single dose of intratracheally instilled PVC dust (< 0.5 μm) in rats, the particles are cleared through the lymphatic circulation and progressively accumulate in the tracheobronchial lymph nodes (Agarwal *et al.*, 1978; Takenaka *et al.*, 1987; Agarwal *et al.*, 1991). Ingested or rectally administered PVC particles were observed within the lymph vessels associated with the intestinal wall of rats, guinea pigs, rabbits, chickens, dogs, and pigs (Volkheimer, 1975). Particles were observed in the blood, bile, urine, and cerebrospinal fluid of dogs, and in the blood of other species, but details of the experimental methods and results were not provided (Volkheimer, 1975). There is no information on the potential bioavailability or biotransformation of PVC.

3.3.1.2 Mammalian Toxicology (Laboratory Animal and Biochemical Studies)

Lethal Effect

PVC is relatively inert and no lethality data have been reported.

Non-Lethal Effects

The weight-of-available-evidence from data generated by inhalation and intratracheal exposure to PVC particles in experimental animals, indicates that PVC itself possesses little or no biological activity, with its physical presence producing benign pneumoconiosis typical of a nuisance dust at elevated dust concentrations (Pigott and Ishmael, 1979; Groth *et al.*, 1981;

Richards *et al.*, 1981; Wagner and Johnson, 1981; Tetley *et al.*, 1981; Agarwal, 1983; Agarwal *et al.*, 1991). Flaws in experimental design, and concomitant exposures to other chemicals raises doubts regarding the significance of earlier studies where animal exposed to PVC dusts by inhalation studies showed pulmonary fibrosis and significant respiratory toxicity (Popow, 1969; Frongia *et al.*, 1974).

Carcinogenicity

Since vinyl chloride has been recognized as a carcinogen (IARC, 1979, 1987), the potential carcinogenicity of PVC has received particular scrutiny (Montgomery, 1982). IARC (1979, 1987) concluded that the evidence that PVC causes cancer was inadequate based on several animal studies, and that the carcinogenicity of PVC was unclassifiable (Oppenheimer *et al.*, 1952, 1955; Kogan and Tugarinova, 1959; Russell *et al.*, 1959; Raikhlin and Kozan, 1961).

3.3.1.3 Epidemiology Studies

Based upon the epidemiological evidence available, exposure to PVC dusts in the work environment can lead to a low grade pneumoconiosis, similar to that experienced with inhalation of other unreactive, nuisance dusts. Chest X-rays of workers often have shown abnormalities, yet these changes have not always been associated with decreased lung function (Miller *et al.*, 1975; Gamble *et al.*, 1975; Lilis *et al.*, 1976; Mastrangelo *et al.*, 1979; Soutar *et al.*, 1980; Chivers *et al.*, 1980; Mastrangelo *et al.*, 1981; Wagoner, 1983; Baser *et al.*, 1985; Ernst *et al.*, 1988; Siracusa *et al.*, 1988; Nielsen *et al.*, 1989; Lee *et al.*, 1991; Ng *et al.*, 1991). The epidemiological data on the respiratory effects of PVC dusts in humans also indicates that such exposure has not produced neoplastic effects. Other studies have investigated the effects of PVC degradation products, particularly following heating or combustion, and are discussed in the Product Category Document entitled "Interpretive Review of the Potential Adverse Effects of Chlorinated Organic Chemicals on Human Health and the Environment - Incineration of Chlorinated Materials -". PVC, under these conditions, can release hydrogen chloride gas or large amounts of carbon monoxide, depending on the oxygen supply (Montgomery, 1982).

Two epidemiological studies that have examined the mortality and cancer incidences of workers in the plastics industry, including PVC fabricators have been conducted (Baxter and Fox, 1976; Chiazze *et al.*, 1977). IARC (1979) concluded that, although there were excesses of certain cancers, these studies were limited in that not all the workers studied were engaged in activities directly involving PVC. In addition, monomeric vinyl chloride, a recognized human carcinogen, was likely present in these work environments. In 1974, it was reported that PVC leaving certain manufacturing plants may have contained as much as 200-400 ppm vinyl chloride (IARC, 1979), current manufacturing technology is capable of producing general PVC which contains less than 1 ppm residual monomer, while modern medical grade PVC is believed to contain less than 10 ppb VCM (Van Dooren, 1991; Thomas and Ramstad, 1992).

3.3.1.4 Exposure Limits

The American Conference of Governmental Industrial Hygienists (ACGIH) considers occupational exposure to PVC dusts under the category Particulates Not Otherwise Classified (PNOC). The threshold limit value (time-weighted average) (TLV-TWA) for this category is

10 mg/m^3 (ACGIH, 1992). The United States Occupational Safety and Health Administration (OSHA) has set limits for inert or nuisance dusts of 15 mg/m^3 (total) and 5 mg/m^3 (respirable), not regulating PVC directly (29 CFR § 1910). Germany, Switzerland, and the United Kingdom have set TLV-TWA limits of PVC (respirable dust) of 5 mg/m^3 (ILO, 1991), as have Sweden and Norway (Norsk Hydro, 1992).

3.3.2 Vinyl Chloride

Vinyl chloride monomer has several synonyms. VCM has also been referred to as chloroethene, chloroethylene, monochloroethylene, and vinyl chloride monomer.

3.3.2.1 Bioavailability, Metabolic Conversion (Pharmacokinetics), and Bioaccumulation

Bioavailability

Based on measured ^{14}C in the urine and expired air, between 70 and 95% of the dose was absorbed following a single oral administration of [^{14}C]VCM (0.05-100 mg/kg body weight) to male rats (IARC, 1979).

The amount of VCM absorbed through the skin is considered to be small. Calculations based on the percutaneous absorption of VCM using Rhesus monkeys indicated that a six-foot, 90 kg man exposed to 7000 ppm (dermal) for two hours would absorb the equivalent of approximately 0.2 ppm (EPA, 1980).

At room temperature, VCM exists as a gas, therefore, inhalation is the most significant route of exposure. Data obtained from the rat indicated that VCM is rapidly absorbed by the lung and readily metabolized (Hefner *et al.*, 1975). Following exposure of male rats to 10 ppm [^{14}C]VCM in the air for six hours, 68% of the radioactivity was excreted in the urine within 72 hours, with approximately 2% exhaled unchanged. Comparatively, exposure to 1000 ppm resulted in a smaller proportion of radioactivity excreted in the urine (56%) and greater portions expired as VCM (12%) (Watanabe *et al.*, 1976; Holmberg, 1984). In a similar system, rats exposed to initial concentrations less than 100 ppm [1,2-^{14}C]VCM in the air absorbed approximately 40% of that inhaled. Within 24 hours, 70% of the radioactivity was recovered in the urine.

Metabolism

Vinyl chloride is metabolized by the cytochrome P450-dependent polysubstrate monooxygenase system (P450) to the reactive epoxide intermediate chloroethylene oxide, which rearranges spontaneously to chloroacetaldehyde (Bolt *et al.*, 1976; IARC, 1979). As reviewed in IARC (1979), the epoxide has also been shown to be capable of reacting with macromolecules such as DNA, RNA, and protein, forming covalently bound adducts (Kappus *et al.*, 1975; Kappus *et al.*, 1976; Bolt and Filser, 1977). These reactions have been elucidated through results obtained with mouse or rat subcellular fractions or P450 inhibitors and inducers, as there are no data yet available for this pathway *in vivo* (Gothe *et al.*, 1974). Chloroacetaldehyde has been shown to combine directly or enzymatically (glutathione S-transferase-mediated) with glutathione to form

S-formylmethylglutathione, which is excreted as N-acetyl-S-(2-hydroxyethyl)cysteine. Chloroacetaldehyde is also oxidized to chloroacetic acid, which is either excreted as such or bound to glutathione in the form of S-carboxymethyl glutathione (Green and Hathway, 1977; Plugge and Safe, 1977).

Bioaccumulation

As discussed above, VCM is readily metabolized and excreted, therefore, it does not accumulate in biological systems. Metabolism is so rapid that no VCM *per se* has been identified in the tissues of animals following exposure to high concentrations, even though the alkylation of DNA and other macromolecules occurred (Watanabe *et al.* 1976; Bergman, 1982). Following dosing of rats with [^{14}C]VCM via inhalation and oral routes, between 2-15% of the radioactivity was measured in the carcass after 72 hours (IARC, 1979), however, the identity of the compounds containing the radioactivity was unknown.

Excretion

In rats, the majority of VCM absorbed by the body is excreted in the form of highly water-soluble metabolites by the kidneys, with up to 70% of the radioactivity associated with a dose f [^{14}C]VCM being recovered in the urine within 24 hours (Watanabe *et al.*, 1976; Bolt *et al.*, 1976). Metabolites that were not excreted in the urine were partly excreted via the feces and partly via expiration of $^{14}CO_2$ (Green and Hathway, 1975; Bolt *et al.*, 1976)

3.3.2.2 Mammalian Toxicology (Laboratory Animal and Biochemical Studies)

Lethal Effects

VCM does not cause acute lethality except at very great doses. The two-hour LC_{50} of VCM for rats, mice, guinea pigs, and rabbits ranges from 113000 to 230000 ppm (294 to 595 g/m^3) (IARC, 1979). Vinyl chloride gas produces narcosis or anesthetic effects, with death following extreme exposures being preceded by excitement, contractions and convulsions, accelerated respiration, and respiratory failure. Microscopically, acutely lethal doses are associated with congestion of the internal organs, with intense damage to the lungs, liver, and kidneys (IARC, 1979). Hepatotoxicity is observed laboratory animals after single, high but nonlethal exposures (Prodan *et al.*, 1975). The induction of cytochrome P450 mixed function oxidase enzyme systems, and the depletion of hepatic glutathione stores prior to exposure enhances the hepatotoxic effects of VCM (IARC, 1979). This effect is of particular interest in interpreting effects from chronic exposures at low doses in both animals and in humans.

Non-Lethal Effects

Teratogenicity

VCM is not teratogenic in mice, rats, or rabbits exposed via inhalation to air concentrations of 500 ppm, 6000 ppm, and 2500 ppm during the period of major organogenesis (EPA, 1987). In some cases, inconclusive findings of increased fetal deaths or minor skeletal variations have been

reported; however, these findings occurred only at levels producing maternal toxicity (EPA, 1984).

Carcinogenicity

Based on studies involving a number of species exposed by various routes (Viola *et al.*, 1971; Holmberg *et al.*, 1976; Maltoni *et al.*, 1981), it was concluded that there is sufficient evidence for carcinogenicity to animals (IARC, 1979, 1987). Vinyl chloride administered orally or by inhalation to mice, rats and hamsters produced an increased tumor incidence in the mammary gland, lung, Zymbal gland, and skin, in addition to hepatocellular carcinomas and angiosarcomas of the liver. In one study, a combination of orally administered ethanol and inhalation of VCM resulted in more liver tumors (including angiosarcomas) than after treatment with VCM alone (Radike *et al.*, 1981). The most comprehensive and in-depth investigation of VCM carcinogenicity (Maltoni *et al.*, 1981) concluded: i) VCM induced tumors in all species and strains of animals tested; ii) tumors of different types were induced at different sites; iii) angiosarcoma of the liver occurred in all species of animal tested; iv) VCM was carcinogenic by inhalation and ingestion, and possibly by injection; v) obvious dose-response relationships were observed for both ingestion and inhalation experiments; vi) treatment duration and schedule markedly affected the neoplastic response, as did the species strain, and sex of the animals tested; vii) neonatal animals were highly responsive; viii) VCM acted as a transplacental carcinogen; and ix) it was carcinogenic at very low exposure levels (*i.e.*, 50 ppm and lower) (Calabrese and Kenyon, 1991).

Mutagenicity

Vinyl chloride vapor induces reverse mutations in a number of *Salmonella typhimurium* strains in the presence of an activation system (*i.e.*, 9000 x g supernatant of rat liver). The response was much greater in the presence of activation systems, yet in its absence, VCM was still able to induce mutations. In addition, VCM has been reported to induce reverse mutations in *E. coli*, forward mutations in *Schizosaccaromyces pombe*, mitotic gene conversions in *S. cerevisiae*, and forward mutations in Chinese hamster ovary cells. The fact that these responses occurred in the presence of a metabolic activation system, indicated that a metabolite(s) was predominantly responsible for the observed mutagenicity. Vinyl chloride has also been found to give positive responses in the *Drosophila* sex-linked recessive lethal assay, but negative in other *Drosophila* assays, including those designed to detect translocations, sex chromosome loss, and dominant lethal effects (IARC, 1979; Calabrese and Kenyon, 1991). Recently, workers exposed to VCM at levels of 5 to 500 ppm developed chromosomal aberrations in peripheral blood lymphocytes (IARC, 1987).

The mutagenicity of several possible metabolites of vinyl chloride has also been examined. Chloroethylene oxide was found to be the strongest mutagen among those tested in *Salmonella typhimurium*, *E. coli*, *S. pombe*, *S. cerevisiae*, and V79 Chinese hamster cells. Chloroacetaldehyde was mutagenic in *Salmonella typhimurium* and V79 Chinese hamster cells, while chloroethanol was weakly mutagenic in *Salmonella typhimurium*, and chloroacetic acid was not mutagenic in *Salmonella typhimurium* (IARC, 1979).

3.3.2.3 Mechanisms of Toxicity

Vinyl chloride has been shown to be activated, via P450 mixed function oxidase enzyme systems, to a reactive epoxide intermediate. Hepatotoxicity increases following administration of P450 inducers such as phenobarbital, Aroclor 1254 (a PCB mixture), and hexachlorobenzene (IARC, 1979; Anonymous, 1987). VCM, or metabolites of VCM alkylate N^4-cytidine, N^6-adenosine, and N^7-guanosine of liver DNA in mice (Osterman-Golkar *et al.*, 1977). Therefore, the weight-of-available-evidence indicates that the carcinogenicity of VCM is related to the direct DNA alkylating effects of metabolites of VCM (likely the reactive epoxide intermediate) produced by the P450 mixed function oxidase enzyme system.

3.3.2.4 Epidemiology Studies

Both the International Agency for Research on Cancer and the United States Environmental Protection Agency have concluded that there is sufficient evidence for the carcinogenicity of VCM in humans (EPA, 1987; IARC, 1987). Specifically, VCM is recognized as a causal agent for angiosarcoma of the liver in humans. These conclusions are based on adequate epidemiological evidence from studies of workers who were exposed to extreme concentrations of VCM (*i.e.*, > 100 ppm and possibly as great as 1000 ppm, IARC, 1979) and who were followed for extended periods of time after first exposures (*e.g.*, 20 or more years).

There are also reports of associations between VCM exposures and other malignancies, such as hepatocellular carcinoma (Gokel *et al.*, 1976; Koischwitz *et al.*, 1981; Evans *et al.*, 1983; Langbein *et al.*, 1983), cancer of the brain (Monson *et al.*, 1974; Tabershaw and Gaffey, 1974; Waxweiler *et al.*, 1976; von Reinl *et al.*, 1977; Cooper, 1981; von Greiser *et al.*, 1982), cancer of the lung (Monson *et al.*, 1974; Waxweiler *et al.*, 1976, 1981; Fox and Collier, 1976; von Reinl *et al.*, 1977; Buffler *et al.*, 1979; Heldaas *et al.*, 1984) and cancer of the lymphatic and hematopoietic systems (Tabershaw and Gaffey, 1974; Waxweiler *et al.*, 1976; von Reinl *et al.*, 1977, von Greiser *et al.*, 1982). Other reviews have cast doubts on the strength of the associations between VCM exposure and these other malignancies (ATSDR, 1989). A critical review of the best available epidemiological data, published by Sir Richard Doll (1988), forms the basis for the following assessment of the association between exposures to VCM and various cancers, including hepatic angiosarcoma.

As pointed out by Doll (1988), a number of studies of workers exposed to VCM have demonstrated that excessive exposure is associated with a hazard of angiosarcoma of the liver. However, epidemiological studies of a specific hypothesized association (*i.e.*, VCM exposure and angiosarcoma of the liver) usually simultaneously examine the occurrence of many other health outcomes. In such cases, it is to be expected that a chance finding of a statistically significant association will be found between the study exposure and another outcome in about 1 in 20 comparisons. Therefore, it is important to determine whether the associations observed are in fact causally related to VCM exposures, or due to chance alone.

To address this question, Doll (1988) conducted a critical examination of the epidemiological data from four comparable studies. The criteria used to ensure the studies were comparable were: i) while the exposure levels do not necessarily have to be the same, the observations of the exposed populations occur over a period of time when a clear hazard existed, and ii) the

reference or control populations from which the expected incidence rates were derived should have been as similar as possible to the study population, except for the absence of exposure to VCM.

The four studies that met these criteria for comparability were the following: the national survey for the United Kingdom (UK) (Jones, 1988), the national survey in the U.S. (Environmental Health Associates, 1986), the study of a VCM production/manufacturing facility in Quebec, Canada, (Theriault and Allard, 1981) and a study of a VCM production/manufacturing facility in Italy (Maltoni and Cotti, 1988). All four studies included workers observed for more than 25 year after first exposure. All four studies examined facilities that produced both VCM and PVC, but not the manufacture of PVC products, thus avoiding obscuring the interpretation of the results by marked differences in the levels of exposure to VCM or by the effects of exposures to PVC dusts (see Section 3.2.1.3 on PVC for discussion of such effects). Each of these studies are briefly summarized below:

i) The U.S. study (Environmental Health Associates, 1986) included 10,173 workers from 37 facilities. Exposures began at least one year before December 31, 1972, and the first exposures started in 1942. Except for one facility (955 employees followed till December 31, 1972), follow-up of the workers was conducted to death or until December 31, 1982. A large portion of the workers were observed for 25 or more years after first exposure since approximately 46% first worked in the facility prior to 1955. Doll (1988) considered there were three minor and two major criticisms of this study. The minor criticisms were: i) the list of employees was compiled by the companies without an independent review, ii) it was assumed all employees were white (3% were black), and white race mortality rates were used for comparisons, and iii) 7.3% of the employees could not be followed-up. The major criticisms were: i) mortality rates of the workers were compared to those for white males for the whole country, whereas a significant number of the facilities were in the south, and these comparisons do not enable consideration of the "healthy worker" effect (*i.e.*, a bias in the study population caused by the possibility that those individuals less susceptible to effects on their health from workplace exposures remain in the work force, while those that are more susceptible leave the work force either voluntarily or due to illness), and ii) no causes of death information was available for 97 of the 1,536 deaths in the cohort, and this deficiency was not considered in calculating the disease specific mortality rates. This deficiency could have resulted in underestimation of the standardized mortality ratios by 6.3%.

ii) The UK study (Jones, 1988) evaluated 5,498 workers in the United Kingdom who experienced at least one year of exposure to VCM for at least 25% of each work week over a period between 1940 and 1974 (Jones, 1988). Vital status was evaluated as of December, 1984. Follow-up was completed for 98.9% of the men, and 780 deaths were identified. Minor criticisms of the study included: i) national mortality rates for England and Wales for 5-year age groups over quinquennial periods for 66 causes of death were used as reference comparisons to the incidence rates for different causes of death in the workers. Definitions for the 66 causes of death were added over the observational period, and therefore, not all categories could be compared over all time periods of observation; ii) attempts were made to classify exposures as low, medium or high; however, within the groups the exposures were greater at the beginning than at the

end of the observation period, presumably due to up-grading of the work environment. In addition, workers often moved from one exposure category to another with changes in job specifications. These factors would tend to overestimate the numbers of deaths in the first two exposure categories (Doll, 1988).

iii) The Canadian study (Theriault and Allard, 1981) reported on 1,611 of a total of 1,659 (97.1%) employees who worked between January 1, 1948 and December 31, 1972 at a facility that manufactured VCM and PVC between 1943 and the late 1960s, at which time VCM production ceased but PVC production continued. Detailed occupational and tobacco smoking histories were obtained through union lists and interviews with next-of-kin, and 156 individuals employed for less than 5 years were excluded from the assessment. The workers were divided into three groups: i) exposed to VCM (451 workers); ii) unexposed (870 workers); and iii) others where exposures were uncertain (134 workers), who were excluded from the assessment. Follow-up to determine vital status was closed on December 31, 1977. A total of 59 exposed (75% with >10 years exposure) and 233 unexposed were included in the final assessment, with histological/cytological information sought on all exposed men who died of cancer. Approximately 44% of the workers were observed >25 years from the first exposure. Mortality and causes of death as specified on death certificates for the exposed and unexposed groups were compared after adjusting for calendar period and age; and were compared with the mortality expected for similar sex- and age-groups in Quebec in 1971. The latter procedure may have caused some distortion in the expected numbers of deaths since the comparison rates used did not cover the entire 1948 to 1977 period; however, Doll (1988) considered such distortion was "unlikely to have been large".

The histopathological examinations conducted were considered by Doll (1988) to be particularly valuable in the interpretation of the effects of VCM exposures and showed that all 8 observed liver cancers were angiosarcomas, and one additional cancer was diagnosed as angiosarcoma of the peritoneum. Two cases of angiosarcoma had also been certified as hepatic cirrhosis. The relative risk of death from all causes was 0.95, showing the "healthy worker" effect (Doll, 1988).

iv) The Italian study (Maltoni and Cotti, 1988) focused on workers from nine VCM and PVC production facilities in Italy. The study was incomplete in 1988, therefore, the Doll (1988) review followed workers up to 1983 from two production facilities which began operations in 1953 (457 and 181 men in each plant). The expected numbers of deaths were estimated by multiplying the person-years at risk by the corresponding national mortality rates for each 5-year age group and 5-year period of the study. The expected deaths amounted to 12.4 and 12.8%, respectively, of the workers in the two plants. A total of four deaths from liver cancer was observed in the cohort. Doll (1988) excluded from his analysis, the information from a third Italian facility because the follow-up period covered fewer than 24 years, and only 3.9% of the cohort of workers was expected to have died.

A follow-up to the Italian study was published by Pirastu *et al.* (1990), indicating that extreme VCM exposures of workers were associated with significant increases in both liver angiosarcomas and hepatocellular carcinomas. Considerable animal data and human

studies on the drug Thorotrast are quoted by the authors as supporting evidence for a relationship between VCM exposure and hepatocellular carcinoma, in addition to angiosarcomas. However, no reference is made to the marked hyperproliferative effects observed in laboratory animals following extreme exposures to VCM (Feron *et al.*, 1981) and the documented evidence between hepatocellular hyperproliferation and hepatocellular carcinomas in rodents (Popper and Thomas, 1975). In addition, the numerous vagaries associated with death certificate diagnosis of particular types of cancers, as pointed out by Doll (1988), raise concerns regarding the data presented by Pirastu *et al.* (1990). It would appear that the weight-of-available-evidence remains in agreement with the conclusions reached by Doll (1988) that the primary carcinogenic effects of VCM are related to liver angiosarcoma. Although hepatocellular carcinomas may be associated with extreme exposures to VCM, it would appear that their occurrence is more likely secondary to concurrent hepatocellular hyperproliferation.

A number of other studies were also available on Norwegian, Swedish, German, French and Japanese workers (Doll, 1988) that contributed supporting evidence, but exhibited a variety of factors that reduced the interpretability of the data (*e.g.*, inadequate follow-up of cohort members, exposures to a variety of other chemicals in addition to VCM and PVC, lack of comparative mortality statistics for the reference populations during the critical period of worker exposures and mortality).

From the analyses of the four main studies, using the remaining studies as supporting information, Doll (1988) reached two major conclusions: i) Apart from liver cancer, the overall mortality of the VCM/PVC workers exposed between the 1940s/1950s and mid-1970s was what would be expected in industries that do not have unusual hazards of accident or disease. The standard mortality ratios (SMR) of approximately 84 were considered typical of causes of death other than cancer, considering the "healthy worker" effect. The SMR of 102 for all cancer other than cancer of the liver, was considered compatible with the absence of increased risk; ii) Workers exposed to VCM concentrations of "several hundred parts per million or more" clearly showed an increased risk of contracting angiosarcoma of the liver, normally an extremely rare disease (annual incidence of 1 to 2 x 10^{-7} in the general population; Byren and Holmberg, 1975). Since death certificates are considered highly unreliable in identifying certain types of cancers, Doll (1988) assumed that the 7-fold excess found for all liver cancers combined was all due to an excess of angiosarcomas. In the four major studies examined, approximately 2% of the deaths observed were attributable to angiosarcoma of the liver.

Doll concluded that it was "difficult to decide whether vinyl chloride produces a risk of developing cancer other than angiosarcoma of the liver which might be small compared to the risks produced by nonoccupational causes, at sites other than the liver" (Doll, 1988, p. 73). He did conclude there was no evidence to support the association between exposure to VCM and any other digestive tract cancer. There was insufficient evidence available, however, to confirm or refute associations between occupational exposures to VCM and cancer of the thyroid, the lymphatic and hematopoetic systems, the brain and melanoma. With respect to the association of exposure to VCM and lung cancer, Doll (1988) concluded that a small hazard may have existed when occupational exposures to VCM were extreme, but that the study data did not conclusively demonstrate this risk and that the increased risk would in any case be negligible at current small exposures to VCM.

Doll also concluded that, since VCM is a proven mutagen and carcinogen in laboratory studies, and a carcinogen to humans, the minute exposures that would result from emissions escaping from VCM facilities must cause comparably minute risks to the general public. The concentrations of VCM measured near VCM/PVC production/manufacturing facilities are in the order of 10 to 40 ppb (EPA, 1975b; Baxter *et al.*, 1977), or some 10,000-fold less than the several hundred or more ppm exposures that resulted in measurable occupational hazards. Therefore, an increased risk of cancer in the general public could not possibly be detected, with the possible exception of an increased risk of angiosarcoma of the liver. Any inference that angiosarcoma incidence in the general population is related to VCM exposure, however, could be misleading because angiosarcoma may also be caused by thorium dioxide and arsenic in pesticides and by certain medicines (Doll, 1988).

No cases of angiosarcoma were detected in populations living near VCM or PVC production facilities in Yugoslavia and Sweden (Saric *et al.*, 1976; Elinder *et al.*, 1981). In the UK, one case out of a total of 14 angiocarcinoma, as diagnosed over a 12 year period in a man who lived half a kilometer from a PVC manufacturing facility. In New York state, 6 of 19 cases of angiosarcoma were in people living within 1 mile of facilities using or manufacturing VCM (Baxter *et al.*, 1977). However, more detailed examination of the 6 "neighbourhood" cases showed that 2 could not be attributed to VCM because the men only lived near the facilities for 6 and 8 years before diagnosis is, respectively, a time period too short for the induction period needed for angiosarcoma. Therefore, Doll (1988) concluded that the discovery of four cases of angiosarcoma in people who lived near facilities that used VCM indicated there may have been a minute hazard to the general public from the VCM concentrations historically observed around manufacturing facilities. However, the concentrations of VCM around production facilities has decreased substantially since the 1970s. VCM air concentrations within a few hundred meters of VCM areas were below analytical detection limits (approximately 5 ppb) for three of five facilities in the UK, and the concentrations for the other two facilities were about 20 ppb (100 m outside the boundary fence), and 88 ppb (just inside the boundary fence). However, accidents and production start-ups were associated with higher concentrations (Turner *et al.*, 1984). Based on this evidence, Doll (1988) concluded that "according to any reasonable criterion, the hazard to the general public (if there is any at all) must be negligible".

3.3.2.5 Exposure Limits

The U.S. EPA has published several estimates of the potential carcinogenic potency (q_1^*) of VCM, based on the application of the linearized multistage model for dose-response extrapolation of data from various laboratory animal studies. In 1980, a q_1^* value of 0.0174 $(mg/kg\ body\ weight/day)^{-1}$ was calculated based on preliminary data from laboratory rats exposed to 10,000 ppm VCM. In 1985, this q_1^* value was modified to 0.0295 $(mg/kg\ body\ weight/day)^{-1}$ using the lung and liver cancer incidence from rats exposed to 30,000 ppm VCM for one year. In 1987, the EPA Carcinogen Assessment Group calculated a potency slope of 2.3 $(mg/kg\ body\ weight/day)^{-1}$ based on the liver cancer incidence of a 143-week study on rats exposed orally to doses of 0-17 mg/kg body weight/day (5 days/week) (ATSDR, 1989). These three cancer potency slope estimates translate into RsD (Risk Specific Dose) values of 0.575, 0.339 and 0.00435 $\mu g/kg$ body weight/day, respectively, at a lifetime risk of one per 100,000, a range of 132-fold.

With respect to occupational limits, the American Conference of Governmental Industrial Hygienists (ACGIH) has recommended a Threshold Limit Value (TLV) of 5 ppm (12.8 mg/m^3) Time-Weighted Average (TWA) (ACGIH, 1991), while a workplace standard of 1 ppm TWA was set by the Occupational Safety and Health Administration (OSHA) (ATSDR, 1989; Calabrese and Kenyon, 1991).

3.4 Aquatic Wildlife Hazard Assessment

3.4.1 Lab Studies

Goldfish exposed to automotive upholstery fabric made from polyvinyl chloride immersed in water exhibited a variety of toxic effects such as, hyperactivity, sluggishness, disoriented swimming, aimless drifting and complete mortality in 24 hour (Ahrens *et al.*, 1978) . Histopathological examination demonstrated congestion, degeneration and haemorrhage in the smaller blood vessels, particularly in the gills, as well as swollen edematous lamellae. Gas chromatography/mass spectrometric analysis identified the major component of the extract of the fabric as triphenyl phosphate. These results suggested that triphenyl phosphate was the compound released from PVC fabric that caused toxic effects in the goldfish, and no evidence was provided to implicate PVC or VCM in the effects observed.

No further information on the toxic effects of PVC was identified.

3.5 Terrestrial Wildlife Hazard Assessment

No information was identified specifically on the potential effects of VCM or polyvinyl chloride on terrestrial wildlife. However, the responses of other terrestrial species would be expected to be similar to those demonstrated in the large number of studies on various laboratory animals.

3.6 Other Environmental Effects

Since the environmental fate characteristics of VCM indicate it is rapidly transformed in the environment, there would be little opportunity for effects on the physical environment by VCM *per se*.

3.7 Significance of Environmental Concentrations

The evidence reviewed demonstrates that the potential carcinogenicity, as indicated by evidence from occupationally exposed populations, is the primary environmental and human health concern related to VCM. Therefore, the evaluation of the significance of the concentrations of VCM in the environment will focus on the potential risks of cancer based on the premise that exposures that would not result in unacceptable cancer risks would not produce other adverse effects in the environment.

The assessment of potential environmental effects of chemicals are based on a many assumptions. Since these assumptions are inherently conservative to avoid underestimating risks due to rare circumstances, the compounding of a number of conservative or worst-case assumptions means that the absolute point estimates of the risk would tend to be over-estimated,

although by an unknown degree. Comparative or incremental risks between the two or more different scenarios, on the other hand, can be estimated with much greater confidence since the same methodologies are used in addressing each situation and major uncertainties arise from the accuracies in estimating exposures. The assumptions used in the estimation of exposure limits and various exposure modifying factors are common across the scenarios being compared.

Therefore, the assessment of the potential risks from VCM and PVC in the environment, as outlined below, is based on a comparison of the predicted risks, as characterized by different assessment procedures, and associated with exposures to historical, present-day and predicted future concentrations of VCM in the environment.

PVC

Except for pyrolytic breakdown products (addressed in a separate the Product Category document entitled "Interpretive Review of the Potential Adverse Effects of Chlorinated Organic Chemicals on Human Health and the Environment - Incineration of Chlorinated Chemicals -", the potential human health effects of PVC relate to exposures to PVC dusts in work environments. Exposures to such dusts would not be expected to occur outside the work environment. Historically, there were concerns about the measurable concentrations of non-polymerized VCM that could diffuse from materials constructed of PVC, or be released during pyrolysis. Changes in production processes have now resulted in a PVC product where VCM residues are less than 1 ppm; thus alleviating potential concerns related to exposures to VCM diffusing from PVC.

VCM

Environmental Concentrations

Based on the physical/chemical properties and the resulting information on the environmental fate of VCM (*e.g.*, the majority partitioning into air where it is degraded quickly though reactions catalyzed by ultraviolet light), environmental concentrations, and therefore levels of potential exposures to VCM, would be virtually zero at locations remote (*e.g.*, several kilometers) from facilities involving the production, manufacturing and disposal of VCM and PVC. Therefore, the potential environmental and human health concerns related to VCM would be at locations near (within a few kilometers) of its production and use, and not in the general ambient environment.

Since concentrations of VCM in air are greater inside production and manufacturing facilities, the potential magnitude of exposure of workers would be greater than for the general population. Primarily because of greater understanding of the potential risks of angiosarcoma of the liver from VCM exposures, the concentrations of VCM in air in the workplace showed marked decreases from values commonly in the range of 260 to 2600 mg/m^3 (approximately 100 to 1000 ppm) prior to 1955 to concentrations of approximately 13 mg/m^3 (5 ppm) by about 1975.

Further decreases in work environment concentrations have occurred since the mid 1970s. Workplace monitoring data demonstrate that air concentrations in non-production areas of facilities that manufacture and use VCM ranged from <0.25 to 10.5 mg/m^3 (<0.1 to 4.11 ppm)

in 1988, and <0.25 to 2 mg/m^3 (<0.1 to 0.77 ppm) in 1992. In areas of plants involved in production and handling, VCM air concentrations ranged from 35 to 26.5 mg/m^3 (13.5 and 10.34 ppm) in one facility, and 0.5 to 11 mg/m^3 (0.2 to 4.11 ppm) in 1988, decreasing to 0.5 to 2 mg/m^3 (0.2 to 0.77 ppm) in 1992 in another facility (Vinyl Institute, personal communication, 1992). These data represent the greatest air concentrations reported for the four facilities over the 5 year period, 1988 through 1992.

Near (within a few hundred meters) VCM and PVC production and manufacturing facilities, IARC (1979) reported average air concentrations of 44 μg/m^3 (17 ppb) prior to 1979. Other researchers reported a range of 26 to 102 μg/m^3 (10 to 40 ppb) during this same time period (EPA, 1975b; Baxter *et al.*, 1977). Air monitoring data collected after 1975, subsequent to the implementation of more stringent standards for workplace air concentrations, showed air concentrations within a few hundred meters of VCM production/handling areas were below analytical detection limits (approximately 13 μg/m^3 or 5 ppb) for three of five facilities in the UK, and the concentrations for the other two facilities were about 20 ppb (100 m outside the boundary fence), and 88 ppb (just inside the boundary fence) (Turner *et al.*, 1984).

Potential Consequences Associated with Environmental Concentrations of VCM

Based on the weight-of-available-evidence demonstrating the rapid dispersion and degradation of VCM in the atmosphere, and that the air concentrations measured near (within a kilometre) of VCM/PVC production/manufacturing facilities are below analytical detection limits (*e.g.*, <5 ppb), exposures of the general public to VCM remote from such facilities would be virtually zero. A similar conclusion was reached by Doll (1988) regarding potential cancer risks to the general public from potential exposures to VCM emissions from production/manufacturing facilities. Very low exposures may be associated with VCM produced from the degradation of other chlorinated organic chemicals from natural and man-made sources (*e.g.*, 1,1,1-trichloroethane and 1,1-dichloroethane); however, no measurable health risks would be expected from such sources.

The question of potential risks to the general public living very near VCM production/manufacturing facilities remains to be addressed. The various risk estimates from exposures to the VCM concentrations observed near production/manufacturing facilities, based n the application of the various EPA cancer potency estimates for VCM, and the cancer incidence rates reported in workers exposed to VCM are summarized in Table 3-1. The first point arising from the various risk estimates in Table 3-1 is the large variation in risks estimated by the different methods. The most recent EPA exposure limit (0.00435 μg/kg body weight/day) (Calabrese and Kenyon, 1991) results in risk estimates at least 9800-fold greater than estimated by simple linear extrapolation of the cancer mortality observed in workers exposed to VCM concentrations of 100 to 1000 ppm to those observed near production/manufacturing facilities (*e.g.*, 10-40 ppb in the mid 1970s and <5 ppb in the mid 1980s). The 1980 EPA cancer potency estimate for VCM results in cancer mortality at least 74-fold greater than those predicted from observations in workers.

The estimates of risks associated with VCM exposures near production facilities as predicted by the EPA cancer potency factors are in stark disagreement with the conclusions of Doll (1988) that the potential risks associated with VCM exposures to the "general public (if there is any at

all) must be negligible". One major reason for this apparent disagreement in potential risks may be related to the large degree of conservatism inherent in the EPA (1987) exposure limit for VCM as estimated using the linearized multistage model. An indication of this conservatism can be obtained through a comparison of the VCM cancer potency estimate derived by extrapolation of liver cancer mortality observed in workers with the various potency estimates of the EPA. This comparison indicates a difference in cancer potency of between approximately 9500- and 95000-fold.

Table 3-1 Cancer Risk Estimates for Near-Plant Air Concentrations of VCM

Cancer Potency Estimate $(mg/kg/day)^{-1}$	Predicted Risks Near-Plant[1] (per 100,000)	
	Air Concentrations 10 - 40 ppb[2] (26 - 102 $\mu g/m^3$)	Air Concentrations <5 ppb[2] (< 13 $\mu g/m^3$)
0.0174[3]	15 - 58	7.4
0.295[4]	25 - 100	13
2.3[5]	2000 - 7700	980
0.00024[6]	0.2 - 0.8	0.1
0.000024[7]	0.02 - 0.08	0.01

(1) Near-plant air concentrations (within a few meters) were 26 to 102 $\mu g/m^3$ (10 to 40 ppb) in the mid-1970s (Baxter *et al.*, 1977), and <13 $\mu g/m^3$ (<5 ppb) in the mid-1980s (Turner *et al.*, 1984).

(2) Exposure estimates calculated for a 70 kg individual breathing 23 m^3 of air per day. Predicted risk = (estimated exposure) x cancer potency factor.

(3) EPA (1980) cancer potency estimate = 0.0174 $(mg/kg\ body\ weight/day)^{-1}$

(4) EPA (1985) cancer potency estimate = 0.0295 $(mg/kg\ body\ weight/day)^{-1}$

(5) EPA (1987) cancer potency estimate = 2.3 $(mg/kg\ body\ weight/day)^{-1}$

(6) Cancer potency estimate of 0.00024 $(mg/kg\ body\ weight/day)^{-1}$ based on a liver cancer mortality of 2 per 100 (2%) (Doll, 1988), assuming i) an air concentration of VCM in the workplace of 100 ppm (260 mg/m^3) (IARC, 1979), ii) a 70 kg individual breathing 23 m^3 of air per day and iii) a linear dose-response extrapolation {*e.g.*, $[(260 \times 23)/(70 \times 0.02)]^{-1} = 0.00024$}.

(7) Cancer potency estimate of 0.000024 $(mg/kg\ body\ weight/day)^{-1}$ based the same calculations as in [6], except assuming an air concentration of VCM in the workplace of 1000 ppm (2600 mg/m^3) (IARC, 1979) {*e.g.*, $[(2600 \times 23)/(70 \times 0.02)]^{-1} = 0.000024$}.

The greatest uncertainty in the epidemiological data lies in the estimated air concentrations at 100 to 1000 ppm to which the workers were exposed. If the air concentrations of VCM were less than these values, the estimated apparent carcinogenic potency of VCM would be greater. However, even if the VCM air concentrations to which the workers were exposed were as low as 10 ppm (10-fold less than those considered representative according to IARC, 1979), the EPA (1987) cancer potency estimate for VCM of 2.3 $(mg/kg/body\ weight/day)^{-1}$ would over-estimate the risk by approximately 980-fold compared to a cancer potency estimate of 0.00024 $(mg/kg\ body\ weight/day)^{-1}$ calculated from epidemiological data (see Table 3-1). According to the information available, it is highly unlikely that the VCM air concentrations in work environments were < 10 ppm during the 1950s and 1960s, and air concentrations in the range of 100 to several hundred ppm were considered to be more likely (IARC, 1979; Doll, 1988).

If it is assumed that the cancer potency estimates based on the epidemiological data are the more reliable, then the potential risks associated with the air concentrations of VCM predicted near production facilities would be in the range of 0.1 to 0.01 per 100 thousand (1 per million to 1 per 10 million) (Table 3-1). Such risk estimates would be clearly unmeasurable in the general population in any practical sense (*e.g.*, a study population of several million would be required to obtain reliable estimates of such risk values). This conclusion is in agreement with that Doll (1988) who concluded that "according to any reasonable criterion, the hazard to the general public (if there is any at all) must be negligible" from VCM exposures to the general public.

The above assessment focuses primarily on potential exposures of the general public living near (*e.g.*, within a few kilometers) of VCM production and manufacturing facilities. Since VCM emissions remain almost exclusively in air, and it has a half-life in the environment of only a few days, its concentration in air would decrease rapidly with distance from point sources. Therefore, potential health risks to the general public in regions remote from VCM production and manufacturing facilities would be even more negligible, and certainly unmeasurable. The maintenance of procedures for non-emissive uses of VCM and strict attention to operations to avoid accidental releases will ensure that the current status of no adverse effects on human health and the environment is maintained. In the future, improved production and manufacturing control technologies and attention to accident prevention, in keeping with policies of progressive product stewardship, will continue to reduce emissions of VCM from production and manufacturing facilities. These expected reductions will reduce the releases of VCM to the environment from point production sources, thereby further reducing the already negligible and unmeasurable risks predicted from current environmental concentrations of VCM near production and manufacturing facilities.

CHAPTER 4 REFERENCES

4.1 References

29 CFR § 1910. (U.S.) Code of Federal Regulation. Title 29 Part 1910.

ACGIH. (1991). *Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices, 1991-1992.* ACGIH, Cincinnati, OH 45211-4438.

ACGIH. (1992). *Threshold Limit Value for Chemical Substances and Physical Agents and Biological Exposure Indices, 1992-1993.* ACGIH, Cincinnati, OH.

AGARWAL, D.K. (1983). Biochemical assessment of the bioreactivity of intratracheally Administered Polyvinyl Chloride Dust in Rat Lung. *Chem. Biol. Interact.* **44**, 195-201.

AGARWAL, D.K., KAW, J.L., SRIVASTAVA, S.P., AND SETH, P.K. (1978). Some biochemical and histological changes induced by polyvinyl chloride dust in rat lung. *Environ. Res.* **16**, 333-341.

AGARWAL, D.K., DOGRA, R.K.S., AND SHANKER, R. (1991). Pathobiochemical response to tracheobronchial lymph nodes following intratracheal instillation of polyvinylchloride dust in rats. *Arch. Toxicol.* **65**, 510-510.

Ahrens, V.D., Henion, J.D., Maylin, G.A., Leibovitz, L., St. John, L.E., Jr., and Lisk, D.J. (1978). A water-extractable toxic compound in vinyl upholstery fabric. *Bull. Environ. Contam. Toxicol.* **20**, 418-422.

ANON. (1972). *Fire Protection Guide on Hazardous Material.* Fourth Edition, Boston, Mass., National Fire Protection Association, pp.325M-137, 49-226-49-227. Cited In: IARC, 1979.

ANONYMOUS. (1987). A scientific basis for the risk assessment of vinyl chloride. *Regul. Toxicol. Pharmacol.* **7**, 120-127.

ATSDR. (1989). *Toxicological Profile for Vinyl Chloride.* ATSDR/TP-88/25, August 1989.

BAIRD, R., GUTE, J., JACKS, C., JENKINS, R., NEISESS, L., SCHEYBELER, B., VAN SLUIS, R., AND YANKO, W. (1983). Health effects of water reuse: A combination of toxicological and chemical methods for assessment. In *Water Chlorination: Environmental Impact and Health Effects.*

BARNES, A.W. (1980). Vinyl chloride and the production of PVC. *Proc. Roy. Soc. Med.* **69**, 277-281.

BARRIO-LAGE, G., PARSONS, F.Z., NASSER, R.S., AND LORENZO, P.A. (1986). Sequential dehalogenation of chlorinated ethenes. *Environ. Sci. Technol.* **20**, 96-99. Cited In: Vinyl Institute, 1990.

BASER, M.E., TOCKMAN, S., AND KENNEDY, T.P. (1985). Pulmonary Function and Respiratory Symptoms in Polyvinylchloride Fabrication Workers. *Am. Rev. Respir. Dis.* **131**, 203-208.

BAXTER, P.J., AND FOX, A.J. (1976). Angiosarcoma of the liver in PVC fabricators. *Lancet* **I**, 245-246.

BAXTER, P.J., ANTHONY, P.P., MACSWEEN, N.M., SCHEUER, P.J. (1977). Anglosarcoma of the liver in Great Britain. *Br. Med. J.* **1**, 919-921. Cited In: Doull *et al.*, 1988.

BERGMAN, K. (1982). Reactions of vinyl chloride with RNA and DNA of various mouse tissues *in vivo*. *Arch. Toxicol.* **49**, 117-129.

BOLT, H.M., AND FILSER, J.G. (1977). Irreversible binding of chlorinated ethylenes to macromolecules. *Environ. Health Perspect.* **21**, 107-112.

BOLT, H.M., KAPPUS, H., BUCHTER, A., AND BOLT, W. (1976). Disposition of [1,2-^{14}C]vinyl chloride in the rat. *Arch. Toxicol.* **35**, 153-162.

BUFFLER, P.A., WOOD, S., EIFLER, C., SUAREZ, L., AND KILLIAN, D.J. (1979). Mortality experience of workers in a vinyl chloride monomer production plant. *J. Occup. Med.* **21**, 195-203.

BYREN, D., AND HOLMBERG, B. (1975). Two possible cases of angiosarcoma of the liver in a group of Swedish vinyl chloride workers. *Ann. NY Acad. Sci.* **246**, 249-250. Cited In: Doull *et al.*, 1988.

CALABRESE, E.J., AND KENYON, E.M. (1991). *Air Toxics and Risk Assessment.* Lewis Publisher, Inc., Chelsea, MN.

CHIAZZE, L., NICHOLS,W.E., AND WONG, O. (1977). Mortality among employees of PVC fabricators. *J. Occup. Med.* **19**, 623-628.

CHIVERS, C.P., LAWRENCE-JONES, C., AND PADDLE, G.M. (1980). Lung Function in Workers Exposed to Polyvinyl Chloride Dust. *Br. J. Ind. Med.* **37**, 147-151.

COOPER, W.C. (1981). Epidemiologic study of vinyl chloride workers: Mortality through December 31, 1972. *Environ. Health Perspect.* **41**, 101-106.

CSDHS. (1990). *Organic Chemical Contamination of Small Public Water Systems in California. Small Water System AB 1803 Final Status Report.* California State Department of Health Services (CSDHS), Office of Drinking Water.

DAVIS, J.W., AND CARPENTER C.L. 1990. The aerobic biodegradation of vinyl chloride in groundwater samples. *Appl. Environ. Microbiol.* **56**, 3878-3880.

DILLING, W.L., TEFERTILLER, N.B. AND KALLOS, G.J. (1975). Evaporation rates of methylene chloride, chloroform, 1,1,1-trichloroethane, trichloroethylene, tetrachloroethylene and other chlorinated compounds in dilute aqueous solutions. *Environ. Sci. Technol.* 9(9), 833-838. Cited In: EPA, 1979.

DOLL, R. (1988). Effects of exposure to vinyl chloride. *Scand. J. Work Environ. Health* 14, 61-78.

ELINDER, C.G., AND PERSHAGEN, G. (1981). *Pilot Study Concerning the Mortality in Njurunda Community.* Swedish Nature Conservancy Board, 1978. Cited In: Doull *et al.*, 1988.

ENVIRONMENTAL HEALTH ASSOCIATES. (1986). *An Update of an Epidemiological Study of Vinyl Chloride Workers 1942-82: Final Report to the Chemical Manufacturers Association.* Environmental Health Associates, Oakland, CA. Cited In: Doull *et al.*, 1988.

EPA. (1974). *Preliminary Assessment of the Environmental Problems Associated with Vinyl Chloride and Polyvinyl Chloride.* (U.S.) Environmental Protection Agency, Washington, DC. Cited In: IARC, 1979.

EPA. (1975a). *Scientific and Technical Assessment Report on Vinyl Chloride and Polyvinyl Chloride.* pp. 7-42. (U.S.) Environmental Protection Agency, Springfield, Va, NTIS EPA-600/6-75-004. Cited In: IARC, 1979.

EPA. (1975b). *Standard Support Document and Environmental Impact Statement: Emission Standard for Vinyl Chloride.* (U.S.) Environmental Protection Agency, Washington, DC. Cited In: Doull *et al.*, 1988.

EPA. (1975c). *Preliminary Study of Selected Potential Environmental Contaminants - Optical Brighteners, Methyl Chloroform, Trichloroethylene, Tetrachloroethylene, Ion Exchange Resins.* p. 286. (U.S.) Environmental Protection Agency (Office of Toxic Substances), Washington, DC EPA 560/2-75-002. Cited In: EPA, 1979.

EPA. (1977). *National Emission Standards for Hazardous Air Pollutants. Standard for Vinyl Chloride.* (U.S.) Environmental Protection Agency. Federal Register 41, 46560-46573. Cited In: IARC, 1979.

EPA. (1979). *Water-Related Environmental Fate of 129 Priority Pollutants.* Volume II. (U.S.) Environmental Protection Agency, Washington, DC. PB80-204381.

EPA. (1980). *Ambient Water Quality Criteria for Vinyl Chloride.* (U.S.) Environmental Protection Agency, Washington, DC.

EPA. (1984). *Health Effects Assessment of Vinyl Chloride.* (U.S.) Environmental Protection Agency. EPA/540/1-86/036.

EPA. (1985). *Final Draft for the Drinking Water Criteria Document on Vinyl Chloride.* (U.S.) Environmental Protection Agency. TR-540-162. Cited in: EPA, 1987.

EPA. (1986). *Quality Criteria for Water, 1986.* (U.S.) Environmental Protection Agency, Office of Water Regulations and Standards, Washington, DC. PB87-226759.

EPA. (1987). *Health Advisory for 25 Organics.* (U.S.) Environmental Protection Agency. Office of Drinking Water (3/31).

EPA. (1991). *Federal Register. Part II Environmental Protection Agency. 40 CFR Part 131 Amendments to the Water Quality Standards Regulation.* (U.S.) Environmental Protection Agency. November 19, 1991.

EPA. (1992). *1990 Toxics Release Inventory Public Data Release.* (U.S.) Environmental Protection Agency, Office of Pollution Prevention and Toxics (TS-779), Washington, DC.

ERNST, P., DE GUIRE, L., ARMSTRONG, B., AND THERIAULT, G. (1988). Obstructive and restrictive ventilatory impairment in polyvinylchloride fabrication workers. *Amer. J. Ind. Med.* 14, 273-279.

EVANS, D.M.D., WILLIAMS, W.J., AND KUNG, I.T.M.(1983). Angiosarcoma and hepatocellular carcinoma in vinyl chloride workers. *Histopathology* 7, 377-388.

FERON, V.J., HENDRIKSEN, C.F.M., SPEEK, A.J., TIL, H.P., AND SPIT, B.J. (1981). Lifespan oral toxicity study of vinyl chloride in rats. *Food Cosmet. Toxicol.* 19, 317-333.

FOX, A.J., AND COLLIER, P.F. (1976). Low mortality rates in industrial cohort studies due to selection for work and survival in the industry. *Br. J. Prev. Soc. Med.* 30, 225-230.

FRONGIA, N., SPINAZZOLA, A., AND BUCARELLI, A. (1974). Experimental lung damage from prolonged inhalation of airborne PVC dust (Italian). *Med. Lav.* 65, 321-342.

GAMBLE, J., LIU, S., MCMICHAEL, A.J., AND WAXWEILER, R. (1975). Effects of occupational and non-occupational factors on the respiratory system of vinyl chloride and other workers. *J. Occup. Med.* 18, 659-670.

GENDRON, L. (1981). *The Clean Air Act - Compilation of Regulations and Guidelines. Fiche.* Air Pollution Control Directorate. EPS 1-AP-81-1.

GOKEL, J.M., LIEBEZEIT, E., AND EDER, M. (1976). Hemangiosarcoma and hepatocellular carcinoma of the liver following vinyl chloride exposure. A report of two cases. *Virchows Arch. (A)* 372, 195-203.

GOODENKAUF, O., AND ATKINSON, J.C. (1986). Occurrence of volatile organic chemicals in Nebraska ground water. *Ground Water* 24(2), 231-233.

GORDON, S.J., AND MEEKS, S.A. (1977). A study of gaseous pollutants in the Houston, Texas area. *Am. Inst. Chem. Eng. Symp. Ser.* 73, 84-94. Cited In: IARC, 1979.

GOTHE, R., CALLEMAN, C.J., EHRENBERG, L., AND WACHTMEISTER, C.A. (1974). Trapping with 3,4-dichlorobenzenethiol of reactive metabolites formed *in vitro* from the carcinogen vinyl chloride. *Ambio* 3, 234-236.

GREEN, T., AND HATHWAY, D.E. (1975). The biological fate in rats of vinyl chloride in relation to its oncogenicity. *Chem. Biol. Interact.* 11, 545-562.

GREEN, T. AND HATHWAY, D.E. (1977). The chemistry and biogenesis of the S-containing metabolites of vinyl chloride in rats. *Chem. Biol. Interact.* 17, 137-150.

GREENPEACE. (1991a). *Chlorine. The Product is the Poison. Part I.* Greenpeace Report.

GREENPEACE. (1991b). *Chlorine. The Product is the Poison. Part II.* Greenpeace Report.

GRIBBLE, G.W. (1992). Naturally occurring organohalogen compounds - A survey. *J. Nat. Prod.* 55(10), 1353-1395.

GROTH, D.H., LYNCH, D.W., MOORMAN, W.J., STETTLER, J.E., LEWIS, T.R., WAGNER, W.D., AND KOMMINENI, C. (1981). Pneumoconiosis in animals exposed to poly(vinyl chloride) dust. *Environ. Health Perspect.* 41, 73-81.

HARTMAN, S., DEBONT, J.A.M., TRAMPER, J., AND LUYBEN, K. (1985). Bacterial degradation of vinyl chloride. *Biotechnol. Lett.* 7, 383-388.

HEFNER, R.E., WATANABE, P.G., AND GEHRING, P.J. (1975). Preliminary studies on the fate of inhaled vinyl chloride monomer in rats. *Ann. NY. Acad. Sci.* 246, 135-148.

HELDAAS, S.S., LANGARD, S.L. AND ANDERSEN, A. (1984). Incidence of cancer among vinyl chloride and polyvinyl chloride workers. *Br. J. Ind. Med.* 41, 25-30.

HILL, J., KOLLIG, H.P., PARIS, D.F., WOLFE, F.L, AND ZEPP, R.G. (1976). In *Dynamic Behavior of Vinyl Chloride in Aquatic Ecosystems.* (U.S.) Environmental Protection Agency, (Office of Research and Development), Athens, Georgia. EPA 600/3-76-001. Cited In: EPA, 1979.

HOLMBERG, B. (1984). The toxicology of monomers of the polyvinyl plastic series. In *Industrial Hazards of Plastics and Synthetic Elastomers.* Alan R. Liss, Inc. New York, NY. pp. 99-112.

HOLMBERG, B., KRONEVI, T., AND WENELL, M. (1976). The pathology of vinyl chloride exposed mice. *Acta Vet. Scand.* 17, 328-342.

IARC. (1979). Vinyl chloride, polyvinyl chloride and vinyl chloride-vinyl acetate copolymers. In *Some Monomers, Plastics and Synthetic Elastomers and Acrolein. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans, Volume 19.* International Agency for Research on Cancer, World Health Organization, Lyon, France.

IARC. (1987). *Overall Evaluations of Carcinogenicity: An Updating of IARC Monographs Volumes 1 to 42.* International Agency for Research on Cancer (IARC) Monographs 19, 377-438.

IJC. (1992) *Sixth Biennial Report on Great Lakes Water Quality.* International Joint Commission, Washington, DC.

ILO. (1991). *Occupational Exposure Limits for Airborne Toxic Substances*, Third Edition, International Labour Office, Occupational Safety and Health Series No. 37.

JONES, R.D. 1988. A mortality study of vinyl chloride monomer workers employed in the United Kingdom in 1940-1984. *Scand. J. Work Environ. Health* In press. Cited In: Doll (1988).

KAPPUS, H., BOLT, H.M., BUCHTER, A., AND BOLT, W. (1975). Rat liver microsomes catalyse covalent binding of ^{14}C-vinyl chloride to macromolecules. *Nature* **257**, 134-135.

KAPPUS, H., BOLT, H.M., BUCHTER, A., AND BOLT, W. (1976). Liver microsomal uptake of [^{14}C]vinyl chloride and transformation to protein alkylating metabolites *in vitro*. *Toxicol. Appl. Pharmacol.* **37**, 461-471.

KIRK-OTHMER. (1983). *Encyclopedia of Chemical Technology. Third Edition, Volume 23, Vinyl Polymers (PVC).* pp. 886-936. Cited In: The Vinyl Institute, 1990.

KIZER, K. (1986). *Final Report on a Monitoring Program for Organic Chemical Contamination of Large Public Water Systems in California. Summary Version.* Department of Health Services, California.

KLEOPFER, R.D., EASLEY, D.M., HAAS, B.B., DEIHL, T.G., JACKSON, D.E., AND WURREY, C.J. (1985). Anaerobic degradation of trichloroethylene in soil. *Environ. Sci. Technol.* **19**, 277-280. Cited In: Vinyl Institute, 1990.

KOGAN, A.K. AND TUGARINOVA, V.N. (1959). On the blastomogenic action of polyvinyl chloride (Russian). *Vop. Onkol.* **5**, 540-545.

KOISCHWITZ, D., LELBACH, W.K., LACKNER, K., AND HERMANUTZ, D. (1981). Angiosarcoma of the liver and hepatocellular carcinomas induced by vinyl chloride. *Fortschr Roentgenstr* **134**, 283-290.

LANGBEIN, G., PERMANETTER, W., AND DIETZ, A. (1983). Hepatocellular carcinoma after vinyl chloride exposure. *Dtsch. Med. Wochenschr.* **108**, 741-745.

LEE, H.S., NG, T.P., AND PHOON, W.H. (1991). Diurnal variation in peak expiratory flow rate among polyvinylchloride compounding workers. *Br. J. Ind. Med.* **48**, 275-278.

LILIS, R., ANDERSON, H., MILLER, A., AND SELIKOFF, I.J. (1976). Pulmonary changes among vinyl chloride polymerization workers. *Chest* **69**, 299-303.

LU, P.Y., METCALF, R.L., PLUMMER, N., AND MANDEL, D. (1977). The environmental fate of three carcinogens: Benzo-(∝)-pyrene, benzidine, and vinyl chloride evaluated in laboratory model ecosystems. *Arch. Environ. Contam. Toxicol.* **6**, 129-142. Cited In: Smith and Dragun, 1984.

MACKAY, D., SHIU, W.Y. AND MA, K.C. (1992). *Illustrated Handbook of Physical-Chemical Properties and Environmental Fate for Organic Chemicals. Volume I. Monoaromatic hydrocarbons, chlorobenzenes, and PCBs.* Lewis Publishers.

MALTONI, C., AND COTTI, G. 1988. Carcinogenicity of vinyl chloride. *Ann. NY Acad. Sci.* **534**, 6-159.

MALTONI, C., LEFEMINE, G., CILIBERTI, A., COTTI, G., AND CARRETTI, D. (1981). Carcinogenicity bioassays of vinyl chloride monomer: a model of risk assessment on an experimental basis. *Environ. Health. Perspect.* **41**, 3-29.

MASTRANGELO, G., MANNO, M., MARCER, G., BARTOLUCCI, G.B., GEMIGNANI, C., SALADINO, G., SIMONATO, L., AND SAIA,B. (1979). Polyvinyl chloride pneumoconiosis: Epidemiological study of exposed workers. *J. Occup. Med.* **21**, 540-542.

MASTRANGELO, G., SAIA, B., MARCER, G., AND PIAZZA, G. (1981). Epidemiological study of pneumoconiosis in the Italian poly(vinyl chloride) industry. *Environ. Health Perspect.* **41**, 153-157.

MERCK. (1989). *The Merck Index. An Encyclopedia of Chemicals, Drugs, and Biologicals.* (S. Budavari, M.J. O'Neil, A. Smith and P.E. Heckelman, Eds.), Eleventh Edition. Merck and Co., Inc. Rahway, New Jersey.

MILLER, A., TEIRSTEIN, A.S., CHUANG, M., AND SELIKOFF, I. (1975). Changes in pulmonary function in workers exposed to vinyl chloride and polyvinyl chloride. *Ann. NY Acad. Sci.* **246**, 42-52.

MOLTON, P.M., HALLEN, R.T. AND PYNE, J.W. (1987). *Study of Vinyl Chloride Formation at Landfill Sites in California.* California State Air Resources Board Contract A4-154-32; NTIS PB87-161279. Cited In: Vinyl Institute, 1990.

MONSON, R.R., PETERS, J.M., AND JOHNSON, M.N. (1974). Proportional mortality among vinyl chloride workers. *Lancet* **2**, 397-398.

MONTGOMERY, R.R. (1982). Polymers. In *Patty's Industrial Hygiene and Toxicology (Third Revised Edition)*. G.D. Clayton and F.E. Clayton, (eds.), Wiley and Sons, New York, NY. pp. 4209-4526.

MORCOS, R. (1988). *Environmental Status Report 1985-1986.* Vinyl Chloride Industry. Environment Canada Report EPS 1/AP/2.

NATIONAL FIELD INVESTIGATIONS CENTER. (1974). *Evaluation of Vinyl Chloride Emissions in the Long Beach Area, California.* EPA/330/2-74/002, Springfield, Va, NTIS. Cited In: IARC, 1979.

NEW YORK STATE DEPARTMENT OF ENVIRONMENTAL CONSERVATION. (1986). *Water Quality Regulations. Surface Water and Groundwater Classifications and Standards.* New York State Codes, Rules and Regulations, Title, Chapter X, Parts 700-705.

NG, T.P., LEE, H.S., LOW, Y.M., PHOON, W.H., AND NG, Y.L. (1991). Pulmonary effects of polyvinyl chloride dust exposure on compounding workers. *Scand. J. Work Environ. Health* **17**, 53-59.

NIELSEN, J., FAHRAEUS, C., BENSYRD, I., WELINDER, H., LINDEN, K., AND SKERFVING, S. (1989). Small airways function in workers processing polyvinylchloride. *Int. Arch. Occup. Environ. Health* **61**, 427-430.

NORSK HYDRO. (1992). *PVC and the Environment*, Ostlands-Posten, Norway.

ONTARIO MINISTRY OF THE ENVIRONMENT. (1991). *Summaries of Rationale Documents for Ontario Air Quality Standards, Tentative Design Standards, Guidelines and Provisional Guidelines.* Ontario Ministry of the Environment, Air Resources Branch.

OPPENHEIMER, B.S., OPPENHEIMER, E.T., AND STOUT, A.P. (1952). Sarcomas induced in rodents by embedding various plastic films. *Proc. Soc. Exp. Biol. NY* **49**, 366-369.

OPPENHEIMER, B.S., OPPENHEIMER, E.T., DANISHEFSKY, I., STOUT, A.P., AND EIRICH, F.R. (1955). Further studies of polymers as carcinogenic agents in animals. *Cancer Res.* **15**, 333-340.

OSTERMAN-GOLKAR, S., HULTMARK, D., SEGERBACK, D., CALLEMAN, C.J., GOTHE, R., EHRENBERG, L., AND WACHTMEISTER, C.A. (1977). Alkylation of DNA and proteins in mice exposed to vinyl chloride. *Biochem. Biophys. Res. Commun.* **76**, 259-266.

PARSONS, F., WOOD, P.R. AND DEMARCO, J. (1984). Transformations of tetrachloroethene and trichloroethene in microcosms and groundwater. *J. Am. Water Works Assoc.* **76**, 56-59. Cited In: Vinyl Institute, 1990.

PARSONS, F.Z., BARRIO-LAGE, G. AND RICE, R. (1985). Bi transformation of chlorinated organic solvents in static microcosms. *Environ. Toxicol. Chem.* **4**, 739-742. Cited In: Vinyl Institute, 1990.

PIGOTT, G.H., AND ISHMAEL, J. (1979). A comparison between *in vitro* toxicity of PVC powders and their tissue reaction *in vivo*. *Ann. Occup. Hyg.* **22**, 111-126.

PIRASTU, R., COMBA, P., REGGIANI, A., FOA, V., MASINA, A. AND MALTONI, C. (1990). Mortality from liver disease among Italian vinyl chloride monomer/polyvinyl chloride manufacturers. *Amer. J. Ind. Med.* **17**, 155-161.

PLUGGE, H. AND SAFE, S. (1977). Vinyl chloride metabolism. A review. *Chemosphere* **6**, 309-325.

POPOW, J. (1969). Effect of poly(vinyl chloride) (PVC) dust on the respiratory system of the rat. *Rocz. Akad. Med. Bialymstoku.* **24**, 5-48.

POPPER, H., AND THOMAS, L.B. (1975). C. Pathology. Alterations of liver and spleen among workers exposed to vinyl chloride. In *Toxicity of Vinyl Chloride - Polyvinyl Chloride*. I.J. Selikoff and E.C. Hammond, (eds.), New York Academy of Sciences, NY. pp. 172-194.

PRODAN, L., SUCIU, I., PISLARU, V., ILEA, E., AND PASCU, L. (1975). Experimental acute toxicity of vinyl chloride (monochloroethene). *Ann. NY Acad. Sci.* **246**, 154-158.

RADDING, S.B., LIU, D.H., JOHNSON, H.L. AND MILL, T. (1977). *Review of the Environmental Fate of Selected Chemicals.* (U.S.) Environmental Protection Agency, (Office of Toxic Substances), Washington, DC. p 147. EPA 560/5-77-003. Cited In: EPA, 1979.

RADIKE, M.J., STEMMER, K.L., AND BINGHAM, E. (1981). Effect of ethanol on vinyl chloride carcinogenesis. *Environ. Health Perspect.* **44**, 59-62.

RAIKHLIN, N.T. AND KOZAN, A.H. (1961). On the development and malignization of connective tissue capsules around plastic implants (Russian). *Vop. Onkol.* **7**, 13-17.

RICHARDS, R.J., ROSE, F.A., TETLEY, T.D., COBB, L.M., AND HARDY, C.J. (1981). Effects in the rat of inhaling PVC dust at the nuisance dust level (10 mg/m^3). *Arch. Environ. Health* **36**, 14-19.

ROTH, S.F. (1976). Saran coatings - latex or lacquer? In *Chemical Marketing and Economics Reprints, Staten Island, New York, Chemical Marketing and Economics Division of the American Chemical Society*, pp. 29-36. Cited In: IARC, 1979.

RUSSELL, F.E., SIMMERS, M.H., HIRST, A.E., AND PUDENZ, R.H. (1959). Tumors associated with embedded polymers. *J. Natl. Cancer Inst.* **23**, 305-315.

SAFE DRINKING WATER COMMITTEE. (1977). Drinking Water and Health. p. 794. National Academy of Sciences, Washington, DC. Cited In: IARC, 1979.

SARIC, M., KULCAR, Z., ZORICA, M., AND GELIC, J. (1976). Malignant tumors of the liver and lungs in an area with a PVC industry. *Environ. Health Perspect.* **17**, 644-652.

SAX, N.I. (1986). Chemical review: Vinyl chloride. *Dangerous Properties of Industrial Material Report* **6(4)**, 13-43.

SIRACUSA, A., FORCINA, A., VOLPI, R., MOLLICHELLA, E., CICIONI, C., AND FIORDI, T. (1988). An 11-year longitudinal study of the occupational dust exposure and lung function of polyvinyl chloride, cement and asbestos cement factory workers. *Scand. J. Work Environ. Health* **14**, 181-188.

SMITH, L.R., AND DRAGUN, J. (1984). Degradation of volatile chlorinated aliphatic priority pollutants in groundwater. *Environ. Int.* **10**, 291-298.

SOUTAR, C.A., COPLAND, L.H., THORNLEY, P.E., HURLEY, J.F., OTTERY, J., ADAMS, W.G.F. AND BENNETT, B. (1980). Epidemiological study of respiratory disease in workers exposed to polyvinyl chloride dust. *Thorax* **35**, 644-652.

TABERSHAW, I.R. AND GAFFEY, W.R. (1974). Mortality study of workers in the manufacture of vinyl chloride and its polymers. *J. Occup Med.* **16**, 509-518.

TAKENAKA, S., RITTINGHAUSEN, S., BELLMANN, B., CREUTZENBERG, O., MUHLE, H., AND MOHR, U. (1987). Morphological effects of nuisance dusts on the respiratory system in rats. *J. Aerosol. Sci.* **18**, 717-720.

TETLEY, T.D., ROSE, F.A., AND RICHARDS, R.J. (1981). Biochemical and cellular reaction of PVC paste polymer and latex following intratracheal instillation into rats. *Inflammation* **5**, 137.

THERIAULT, G., AND ALLARD, P. (1981). Cancer mortality of a group of Canadian workers exposed to vinlychloride monomer. *J. Occup. Med.* **23**, 671-676.

THOMAS, J.-C. (1977). PVC and security, European regulations (Fr.). *Caoutch. Plast.* **571**, 33-38. Cited In: IARC, 1979.

THOMAS, V.N., AND RAMSTAD, T. (1992). A dynamic headspace GC method for the determination of vinyl chloride monomer in stored solutions of cefmetazole sodium in PVC bags. *Acta Pharmacol. Nordica* **4**, 97-104.

TORKELSON, T.R. AND ROWE, V.K. (1981). Halogenated aliphatic hydrocarbons containing chlorine bromine and iodine. In *Patty's Industrial Hygiene and Toxicology*. Third Revised Edition. G.D. Clayton and F.E. Clayton, (eds.). John Wiley & Sons.

WATANABE, P.G., MCGOWAN, G.R., MADRID, E.O., AND GEHRING, P.J. (1976). Fate of [^{14}C]vinyl chloride following inhalation exposure to rats. *Toxicol. Appl. Pharamcol.* 37, 49-59.

WAXWEILER, R.J., STRINGER, W., WAGONER, J.K., JONES, J., FALK, H., AND CARTER, C. (1976). Neoplastic risk among workers exposed to vinyl chloride. *Ann. NY Acad. Sci.* 271, 40-48.

WAXWEILER, R.J., SMITH, A.H., FALK, H., AND TYROLER, H.A. (1981). Excess lung cancer risk in a synthetic chemicals plant. *Environ. Health Perspect.* 41, 159-165.7

WESSLING, R.A., AND EDWARDS, F.G. (1971). Vinylidene chloride polymers. In *Encyclopedia of Polymer Science and Technology, Plastics, Resins, Rubbers, Fibres, Volume 14.* N.M. Bikales, (ed.), New York, Interscience, pp. 540-579. Cited In: IARC, 1979.

WOLF, K., HOLLAND, R., AND RAJARATNAM, A. (1987). Vinyl chloride contamination: The hidden threat. *J. Hazard. Natl.* 15, 163-184. Cited In: Vinyl Institute, 1990.