

VINYLDENE CHLORIDE (VDC)

VCCEP

SUBMISSION

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1. Executive Summary

This submission on Vinylidene Chloride (VDC), compiled by The Dow Chemical Company (Dow), is intended to meet all of the requirements of the Voluntary Children's Chemical Evaluation Program (VCCEP) outlined by the Environmental Protection Agency (EPA). As requested by the EPA, an exposure assessment, a hazard assessment, risk assessment and data needs assessment have been completed. Further, background information is also included in order to put the exposure data into perspective. Finally, an assessment of the relevance of the biomonitoring data, which was the primary basis for the inclusion of VDC in the program, is also provided.

Basis for VCCEP Listing

EPA has indicated that VDC's inclusion in the VCCEP was due to its presence in the USEPA Total Exposure Assessment Methodology (TEAM) biomonitoring study as well as in the National Contaminant Occurrence Database (NCOD) and in indoor air. A detailed analysis of the biomonitoring data from the TEAM study suggests that the foundation for inclusion of VDC in the VCCEP is weak. VDC was only occasionally detected or not detected at all in the majority of the studies that were cited. In studies where VDC was detected, a source for the VDC was not readily identifiable. Further, where sources were identified, they were not always found to be accurately reported based on known uses. EPA's use of VDC's presence in the NCOD also provides an incorrect perception of the presence of VDC in various water sources. NCOD data indicate that only 3.4% of surface water samples had detectable amounts of VDC and only 1.3% of groundwater samples had detectable amounts of VDC. Most of the available indoor air data available for VDC is also from the USEPA TEAM study. Overall the pattern of VDC concentrations reported in the early 1980's for indoor air suggests that the high values reflect historical occupational activity that can not be confirmed and is unrelated to current VDC use or production. More recent ambient air monitoring provides the most relevant information. Upon detailed assessment of the cited data sources, the basis for inclusion of VDC in the VCCEP appears to be weak.

Potential VDC Sources

The potential for exposure to VDC has been well characterized. This review includes analyses of the VDC life cycle and customer surveys. A clear picture of potential exposure of humans, and in particular children, to VDC has emerged. Potential sources of exposure are limited and emissions are expected to continue to decline as they have for a number of years. At the present time, VDC is produced solely for use as a chemical intermediate. Applications are largely industrial-based "closed systems" polymer production operations. There is extremely limited potential for consumer exposure since only very low levels of VDC remain in the polymers. One of the greatest potential environmental sources of VDC is via the degradation of 1,1,1-trichloroethane. However, 1,1,1-trichloroethane has been phased out of production under the Montreal Protocol so the levels of VDC in the environment from this source are expected to continue to decline.

Exposure Assessment

Pathways of potential exposure to children were selected by considering physicochemical, life-cycle, usage and hazard data. Applications where VDC is utilized as an intermediate with the final product several steps removed from the consumer were not considered to be plausible exposure pathways. Acute exposures were also not

considered because the most likely potential exposure is to trace levels of VDC, which would not be acutely toxic.

Detailed exposure assessments have been compiled on “inhalation of ambient air”, “ingestion of water”, “ingestion of food that has been in contact with VDC containing polymer food wrap” and “inhalation of residential indoor air as a result of its use in VDC containing latex carpet backing”. The selection of scenarios in each of these assessments provides overly conservative estimates of exposure which results in a screening estimate of risk but does not provide an estimate of actual exposure and risk. Since a distribution or range of exposure values was calculated for each of these scenarios, an estimate of the midpoint or median for these values gives the central tendency for each exposure scenario. These may be interpreted as “typical” exposures for the conservative scenarios. Estimates of the upper end of the distribution or range of exposure values may be interpreted as the high end exposures for the scenarios that were defined to give health protective conservative estimates of exposure.

The assessment shows that only extremely low exposures are anticipated for each of the four scenarios. The central tendency exposure ranged from 0.008 ug/kg/day (drinking water) to 0.024 ug/kg/day (ambient air) with the total calculated to be 0.044 ug/kg/day. The high end exposures ranged from 0.014 ug/kg/day (drinking water) to 0.072 ug/kg/day (ambient air) with the total aggregate exposure calculated to be 0.15 ug/kg/day.

Hazard Assessment

The potential toxicity of VDC has been extensively studied in a variety of assays and in a number of different species of test animals; a substantial hazard database has been accumulated during the past few decades. Data has been generated on categories listed in all three tiers of the VCCEP, and the database includes studies of varying sophistication and range. In many cases, multiple studies are available that individually or collectively provide a complete assessment of a particular VCCEP hazard category for VDC. Conversely, numerous studies have provided data that is applicable to more than one VCCEP category, for example the evaluation of gonads and nervous and immune system tissues in repeated-dose toxicity studies providing assessments of potential reproductive toxicity, neurotoxicity and immunotoxicity, respectively. Further testing to provide comprehensive evaluations of those few remaining categories of tests listed in VCCEP specifically targeted for evaluation in young animals would be dependent upon evidence of significant potential exposure of children. Since significant exposures to children do not occur from existing uses and applications of VDC, further hazard testing is unwarranted.

Risk Assessment

The available VDC exposure and hazard information allow for a reliable risk assessment for children. Four potential sources of VDC exposure of children aged one to eighteen were considered: ambient air, the backing used in some indoor carpeting, drinking water, and migration from plastic wraps into food. Very conservative estimates of exposure were utilized. In the ambient air assessment, only air samples having detectable levels of VDC, <10% of the samples collected, were used to define potential exposure. In the carpet backing assessment, residual (unreacted) VDC content in liquid latex applied to carpets was used, ignoring the % market share of VDC-containing carpets and the significant loss of volatile chemicals that occurs during oven drying of carpets. In the water assessment, it was assumed that all drinking water contains at least the limit of detection levels of VDC in well water analyses. Finally, the maximum levels of monomer in food wraps was assumed in the polymer food wrap assessment. Despite this,

estimated exposures from each potential source or as an aggregate exposure, were several orders of magnitude less than the EPA identified acceptable daily intake of VDC (RfD). Moreover, even worst case aggregate exposure scenarios were 3-4 orders of magnitude lower than the minimally toxic dose levels in animal studies. It is beyond reasonable expectations that a possible age-related sensitivity can exceed this safety margin.

Data Needs Assessment

Just as "Risk" for any compound is determined by the interaction of "Hazard" and "Exposure", the evaluation of data adequacy in meeting the objectives of VCCEP requires the examination of both hazard data and exposure data, including projected future exposure potential. These databases are not exclusive of each other. A lack of potential exposure of a specific population may negate the need for a very focused examination of a particular hazard endpoint. Conversely, the lack of a specific hazardous property may negate need for extensive exposure monitoring of a specific population to a compound. Modeling of worst case, generally unrealistic, scenarios of exposure for a specific population such as children may further place the potential risk posed by a chemical in perspective. **When the hazard and exposure databases for VDC were examined and utilized to model risk, it was concluded that no further exposure monitoring or hazard evaluation studies were warranted given present and anticipated future use conditions.**

2. Basis for VCCEP Pilot Program Listing

2.1 Overview

In listing VDC in the VCCEP Pilot Program, EPA used existing data sources that it believed to be especially relevant to children's chemical exposures, such as the presence of the chemical in human tissues/blood, in food and water children eat and drink and in the air children breathe. For VDC, EPA specifically cites, in the VCCEP Federal Register Notice, (Dec. 26, 2000), Table 1 – *Chemicals Identified for the VCCEP Pilot*, that its presence in the Total Exposure Assessment Methodology (TEAM) biomonitoring study as well as in the NCOD and in indoor air (no specific reference) supported its inclusion in the VCCEP (U.S. EPA, 2000). In the following paragraphs, VDC data in these studies/databases has been summarized along with a discussion of the relevance of this data to inclusion of VDC in this program.

2.2 Biomonitoring Data

2.2.1 Review of Data

As indicated in the Federal Register notice, VDC was included and detected in the U.S. EPA TEAM study. However, as the TEAM study included a number of different evaluations, it should be noted that there were a number of phases of the TEAM study where VDC was essentially not detected or not included because of lack of detection in prior phases.

The TEAM study, carried out between 1979 and 1985, consisted of three different phases. Phase I was a pilot field test of the methodology. The objective of Phase II was to estimate the distribution of exposure to 20 toxic substances for a target population in an industrial/chemical manufacturing area and to carry out smaller studies for population in non-chemical manufacturing areas. The Phase II study included three field trips to both Elizabeth and Bayonne, New Jersey and one each to North Carolina and North Dakota. In a review of the Phase I and Phase II studies, VDC was not categorized as "prevalent" (Wallace, 1987). The data included in the Federal Register VCCEP Notice, Table 2, "Frequency of Detection and Concentration of Select VCCEP Pilot Chemicals in Certain Human Biomonitoring Studies" does not necessarily reflect this assessment by the author. In Table 2, a detection frequency of 95% of 49 samples and a concentration of 6.6 ug/m³ is denoted for VDC (U.S. EPA, 2000). This detection frequency value is only related to data from Phase II of the TEAM study and represents information gathered during only one season, the third season, in the New Jersey sites. The information does not appear to be reflective of the breath data from the previous two seasons in NJ where the detection frequency was 12% in 340 samples in the first season and 22% in 157 samples in the second season. Data from the second and third seasons were derived from subsets of the subjects sampled in the first season; 95% of 49 samples in a group selected as positive detects in the first season. The TEAM study does not comment on the large increase in detection frequency observed in the smaller subset of subjects that were followed into the third season (Wallace, 1987).

It is also important to note that the TEAM study subjects specifically did not include children and intentionally over-sampled occupationally exposed individuals and smokers. This study was also conducted 20 years ago, when there were fewer regulatory controls in place. Further, the samples taken were only breath samples not blood or urine (Wallace, 1987).

The TEAM study attempted to evaluate the relative importance or likelihood of exposure to the target compounds in the air. The TEAM study sorted target compounds into the following four categories based on the percent measurable in breath and air samples in New Jersey over the three seasons: "ubiquitous compounds", "often present",

“occasionally found”, and “never found”. VDC was listed as an “occasionally found” material in all three seasons based on percent measurable: first season 0-12%, second season 8-22%, and third season 1-95% (Wallace, 1987).

A review of the TEAM study data and reports indicates that, in fact, fewer than 7% of the 1085 personal air samples collected from 355 New Jersey residents over the three seasons had measurable concentrations of VDC (Wallace, 1990). The infrequent detection of VDC is noted in EPA's own report of the TEAM study that characterizes VDC as belonging to a class of substances that “were only occasionally found (<10% measurable in most sample types)” (Wallace, 1987). A subsequent EPA publication analyzing results from the TEAM Study similarly states that VDC and two other VOCs are “much less prevalent” and were “measured in only a few percent of the personal and outdoor air samples collected in the TEAM studies” (Wallace, 1990). VDC was not included in Phase III due to low detection frequency in the Phase II studies.

The data summarized in Table 2.2.1.1, on this page, provides further support to the infrequent detection of VDC in breath and air samples (Wallace, 1987). While it was detected more frequently in water samples, it was present at extremely low concentrations (0.05 ng/ml). A full assessment of the significance of the levels found in water is summarized in 5.3.1

Another important element to be considered from the TEAM study is the potential source of the VDC in the personal air samples. In a published summary of the risk associated with compounds in this study, it was noted that VDC in the personal air samples with the highest concentration came from a cabinet maker. For example, the single highest measured exposure to VDC was 120,000 ug/m³ (Wallace, 1991). It was indicated that the exposure came from the use of VDC as a solvent in this occupation. This is either an inaccurate analysis or an isolated incident involving the incorrect use of VDC. Historically, the volatility of VDC has precluded its use as a solvent. To our knowledge, VDC has never been marketed to consumers for use as a solvent.

Table 2.2.1.1 TEAM Study Phase II
VDC Quantifiable Limits and Detection Frequency Summary

Study Phases	Sample Type	Min. Quantifiable Limit	Max. Quantifiable Limit	% Measurable	% Measurable/ %Above Max QL
New Jersey: 1 st Season	Overnight Personal Air	5.2 ug/m3	244 ug/m3	2.92	---
	Daytime Personal Air	5.2 ug/m3	236 ug/m3	5.98	2.45
	Breath	4 ug/m3	56 ug/m3	12.0	6.78
	Overnite Outdoor Air	2.88 ug/m3	48 ug/m3	1.26	1
	Daytime Outdoor Air	3.44 ug/m3	31.6 ug/m3	.35	1
	Water	0.05 ng/ml	0.05 ng/ml	40	1
New Jersey: 2 nd Season	Breath Samples	5.18 ug/m3	22.4 ug/m3	59.4	15
	Overnight Personal Air	6 ug/m3	48 ug/m3	9.75	3.34
	Daytime Personal Air	6 ug/m3	48 ug/m3	11	3.08
	Overnite Outdoor Air	3.6 ug/m3	39.2 ug/m3	10.9	0
	Daytime Outdoor Air	6.4 ug/m3	56 ug/m3	8.38	0
	Water	0.05 ng/ml	.05 ng/ml	25.9	
New Jersey: 3 rd Season	Breath	6.6 ug/m3	9.6 ug/m3	94.9	94.9
	Overnight Personal Air	8.4 ug/m3	17.2 ug/m3	2.63	2.63
	Daytime Personal Air	8.4 ug/m3	25. ug/m3	9.25	8.74
	Overnite Outdoor Air	4.4 ug/m3	5 ug/m3	1.29	1.29
	Daytime Outdoor Air	5.6 ug/m3	6 ug/m3	1.29	1.29
	Water	.05 ng/ml	.05 ng/ml	43.5	

2.2.2 Analytical Issues

Numerous researchers, both within and outside of biomonitoring research, have identified potential issues when analyzing for low levels of VDC in air samples. Accuracy rates as low as 29% have been found in one study, where flame ionization detection (FID) was utilized to analyze ambient air samples (Pleil, et.al.,1988). In this same study, 70% of the samples were recorded as false positives. The researcher concluded that when quality results are needed, FID should only be used as a screening tool; mass spectrometry should be performed to confirm the chemical identity (Pleil, et.al, 1988). In another ambient air study, researchers denoted that the detected levels of VDC did not correlate to known users of VDC in the area. They suggested that the possibility remained that VDC was an artifact and formed either in the atmosphere or during thermal desorption from the TENAX-GC sampler. As it is readily accepted that VDC can be formed by thermal dehydrochlorination of 1,1,1-trichloroethane and this compound was widely used during this time, this explanation is plausible (Harkov, 1984). In yet another study, it is denoted that VDC is highly volatile; therefore, it breaks through the TENAX monitor after only a portion of the monitoring period. Thus, when the calculation is based on the "breakthrough volume", it could result in an over or underestimate of the actual concentrations. Additionally, the sensitivity is reduced by the same factor (Wallace, 1991). Although not explicitly stated in the report, this probably explains the absence of VDC concentration values for the fraction of air and breath samples reported as containing measurable VDC (Wallace 1987). In the TEAM study, summarized above, given that the breath and outdoor air samples were collected on TENAX-GC cartridges and that higher concentrations of 1,1,1-trichloroethane were detected in such studies, it is plausible that the presence of VDC is due largely from the dehydrochlorination of 1,1,1-trichloroethane.

2.2.3 Relevance

A detailed analysis of the biomonitoring data from the TEAM study suggests that the utilization of this data as a foundation for inclusion of VDC in the VCCEP is weak. As noted above, VDC was only occasionally detected or not detected in the majority of the studies. In studies where there was a higher detection frequency, a plausible source for the VDC was not readily identifiable. Further, where sources were purported, they were not applications to which the industry marketed VDC. Given the physicochemical properties of this compound, it is not feasible for VDC to be incorporated in formulations that would result in such exposures. There were also analytical issues identified that may have contributed to the frequency and levels of VDC detected.

The issues described above as well as the low detection frequency makes the interpretation of risk from biomonitoring data difficult. Many of these factors were also identified in an EPA scientist's review of risk associated with VDC using results from the TEAM study. In this review, it was noted that the population risks of VDC can be calculated, but the interpretation of the risks is difficult (Wallace, 1990). For these reasons, the results of biomonitoring studies have not been included as indicators of actual exposure in the detailed exposure and risk assessment in Sections 5.0 and 7.0 of this report.

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2.3 Indoor Air Review

2.3.1 Indoor Air Monitoring Studies

The first available study that measured VDC was conducted in indoor air in 26 homes and apartments near Research Triangle Park, NC in the early 1980's. VDC was found in 4 of 15 summer samples and 4 of 16 winter samples. No VDC was found in parallel samples taken outdoors. No correlation was found between the presence of VDC in indoor air and structural characteristics of the dwelling or activity. The reported mean concentration of the positive samples, not including samples below the detection levels, was ca.100 $\mu\text{g}/\text{m}^3$ (Pleil 1985 as cited in ATSDR 1994).

A larger study, the USEPA Total Exposure Assessment Methodology (TEAM) study examined indoor, outdoor, personal air and breath samples for several locations in New Jersey and several hundred individuals. The personal air sampler was attached to the individual and included indoor and outdoor exposure. Measurable VDC was found in 77 of 1085 personal air samples (7%) from 355 New Jersey residents taken over three seasons. Estimated 24-hr average exposures of ~ 750 persons in 6 urban areas from the early 1980's were 6.5 $\mu\text{g}/\text{m}^3$ and the air concentration outside 175 homes in 6 urban areas was less than 1 $\mu\text{g}/\text{m}^3$ implying greater indoor exposure to VDC than outdoor exposure to VDC. The Tenax-GC adsorbent had a low breakthrough volume for VDC and only allowed the quantitation of VDC concentrations greater than 3 to 14 $\mu\text{g}/\text{m}^3$. (Wallace 1991)

In an indoor air review article the weighted average geometric mean concentration of VDC in established dwellings is given as between 1 and 5 $\mu\text{g}/\text{m}^3$, the fifth lowest of six indoor air concentration categories. No additional information about this result is given in the review. (Berglund et. al. 1986, as cited in S. K. Brown, et. al. 1994.)

More recently, during June 1990, 125 households in Woodland, California were monitored for a variety of toxic air contaminants (Sheldon et al. 1992 as cited in CalEPA TAC ID List 1997). Woodland (population 50,614) is the county seat of Yolo County, in California's Central Valley. Woodland is located about ten miles north of Davis, and about eight miles west of the Sacramento International Airport. VDC was not present at measurable concentrations in any of the samples. The method quantitation limit for VDC was $0.2 \mu\text{g}/\text{m}^3$.

2.3.2 VDC Concentration in Personal Air Samples

The highest VDC exposure concentration in 1085 personal air samples collected from 355 New Jersey individuals in the TEAM study, was $120,000 \mu\text{g}/\text{m}^3$ for a cabinet maker. The second highest was $14,000 \mu\text{g}/\text{m}^3$, measured for the same cabinet maker in a different season. The 1085 exposure values average $150 \mu\text{g}/\text{m}^3$ (Wallace 1991). Excluding the two highest exposures gives an average of $28 \mu\text{g}/\text{m}^3$ for the remaining 1083 exposure values. Four additional exposures were greater than $1000 \mu\text{g}/\text{m}^3$. Excluding these and the two highest values gives an average exposure of $6.5 \mu\text{g}/\text{m}^3$ for the remaining 1079 values (Wallace 1991). Only 77 of these 1085 samples actually had measurable VDC, another 107 had detectable but not quantifiable concentration of VDC. These 77 samples must have had an average concentration of about $2000 \mu\text{g}/\text{m}^3$. Omitting the six highest values leaves an average of about $100 \mu\text{g}/\text{m}^3$ for the remaining 71 samples. A statewide survey of industries in NJ conducted during the same early 1980's time period was successful at locating only three small to intermediate users of VDC (Harkov 1984). These were considered unlikely to be the source of the relatively high measured VDC concentrations observed.

2.3.3 Discussion

The pattern of high, sporadic, indoor air values observed in the early studies with lower values and nondetects in the later studies is similar to the pattern in the ambient air results (Fontaine 2002a). This sporadically high concentration data suggests a strong but less common source.

The relatively high indoor air concentration of the North Carolina samples (Pleil 1985 as cited in ATSDR 1994) is consistent with a concentrated, nearby or indoor source of VDC. However no current or historical consumer products contain large amounts or high concentrations of VDC and the concurrent outdoor concentrations of VDC in air were less than the detection limit. It is difficult to reconcile these facts without invoking a different source for the measured VDC.

A sporadic occurrence of high values is seen for the personal air samples. The highest personal air samples are orders of magnitude greater than the rest of these samples (Wallace 1991). These concentrations are very high ($120,000$ and $14,000 \mu\text{g}/\text{m}^3$) and suggest a strong source associated with that individual's unique daily activity. It is unlikely that the high values resulted from exposure to bulk monomer because there are no known solvent uses. VDC does not have solvent uses because of its high volatility and its need for stabilizers to prevent peroxide formation and self-polymerization. It is possible that a cabinet maker would use 1,1,1- Trichloroethane to clean hardware or other solvents to strip wood and 1,1,1- Trichloroethane has been suggested as a source of analytical artifacts in the thermal desorption analysis (Harkov, et al. 1984).

Prior to the elimination of dispersive uses of 1,1,1- Trichloroethane by the Montreal Protocol in 1995, it was occasionally detected at higher concentrations in indoor air (Shah and Singh 1988). The historical use of 1,1,1- Trichloroethane in cleaning systems that vent directly to the air could conceivably have provided a source of VDC as its degradation product. Landfills contaminated with other chlorinated organics could also provide a source of VDC as a degradation product. In either case high VDC concentrations could result from the decomposition of 1,1,1- Trichloroethane either in-situ or during thermal desorption of the samples. Thermal desorption of the Tenax GC sorbent was performed at 200 to 250°C and higher chlorinated ethanes have been shown to decompose at these temperatures in the presence of copper metal (Glisson et al. 1986). The studies employing cryogenic trapping and a lower desorption temperature (100°C) gave much lower VDC concentrations in ambient urban air (Grimsrud and Rasmussen 1975, Singh et al. 1982) than those obtained by researchers using higher temperature thermal desorption. Studies using cryogenic sample collection and lower temperature desorption also had lower detection limits for VDC than those obtained using sorption to Tenax GC and higher temperature thermal desorption. The declining frequency of higher ambient air concentrations of VDC occurs during the phase out of 1,1,1- Trichloroethane and during a period when VDC use remains fairly constant. Both of these observations are consistent with 1,1,1- Trichloroethane as the ultimate origin of the high measured values of VDC.

The lack of detectable VDC in the indoor air of the 125 California residences indicates that common consumer products in these homes do not result in indoor air concentrations of VDC greater than the 0.2 µg/m³ detection limit. The exposure assessment for the carpet scenarios (Fontaine 2002b) gave a conservative, health protective estimate of the average indoor air concentration of 0.06 µg/m³. Since carpet has a larger mass compared to other indoor items, it is a potentially larger source and may be considered a worst case.

Overall the pattern of VDC concentration reported in the early 1980's for indoor air, personal air, and outdoor air samples suggests that the high values reflect historical occupational activity unrelated to VDC use or production. Given the large amount of available data obtained over many years and at many locations, ambient air monitoring for VDC provides the best available surrogate for estimating current VDC exposure of both children and adults.

2.3.4 Summary

Most of the available indoor and personal air monitoring data available for VDC is from the USEPA Total Exposure Assessment Methodology (TEAM) study (USEPA 1987). A description of the technical limitations of the VDC biomonitoring data from this study has been given above and these are relevant to the interpretation of the indoor and personal air VDC concentration data. Overall the pattern of VDC concentrations reported in the early 1980's for indoor air, personal air, and outdoor air samples suggests that the high values reflect historical occupational activity unrelated to VDC use or production and that more recent ambient air monitoring provides the best available surrogate for childhood and adult exposure (Fontaine, D.D., 2002c)

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USEPA (1987). Total Exposure Assessment Methodology (TEAM) Study: Elizabeth and Bayonne, New Jersey, Devils Lake, North Dakota and Greensboro, North Carolina. Volume II Part 2. EPA/600/6-87/002b

Wallace, L. A., (1991). Comparison of Risks from Outdoor and Indoor Exposure to Toxic Chemicals. *Environmental Health Perspectives* 95 7-13.

2.4 National Contaminant Occurrence Database (NCOD)

In the Federal Register Notice, the EPA also uses NCOD to support its inclusion of VDC in the VCCEP. NCOD was set up in 1999 to support federal and state drinking water programs. It seeks to document the universe of contaminants that conceivably could come into contact with drinking water. NCOD data indicate that out of 11,810 analyses

of surface waters, only 407 or 3.4% had detectable amounts of VDC. Importantly, the average concentration of those samples that could be quantified was only 2.2 ug/l after the elimination of one extreme value. Similarly, NCOD data indicate that out of 53,236 analyses of ground water, only 690 or 1.3% had detectable amounts of VDC. The average measured level of VDC in the groundwater samples was only 2.5 ug/l. Both of these averages are below the safe drinking water concentration for VDC. Further, it should be noted that NCOD contains occurrence monitoring data from sampling locations throughout a public water system, therefore a detection value does not necessarily mean the contaminant would be found at the tap. This limitation of the NCOD data, together with the extremely limited presence of VDC, illustrate the issues which must be considered in utilizing this information in an exposure assessment. These issues and others will be addressed in Section 5.2.

3. Product Overview

3.1 Manufacturing Process

The production of VDC begins with the chlorination of ethylene dichloride to form 1,1,2-trichloroethane, with a limited amount of 1,1,2,2-tetrachloroethane and 1,1,1,2-tetrachloroethane being produced as byproducts. The VDC is then formed by dehydrochlorination of 1,1,2-trichloroethane with lime or caustic soda. Production occurs in a closed system using a stainless steel reactor system. Air emissions are collected and captured using carbon absorption systems. Waste streams are incinerated. To prevent the formation of explosive peroxides and polymer during shipment and subsequent storage, an inhibitor, monomethyl ether of hydroquinone (MEHQ), is added. Commercial grades contain up to 200ppm of MEHQ.

VDC is primarily shipped in bulk containers, either DOT 105A300W rail cars that are plastic-coated carbon steel or dedicated MC 304/307 trucks that are stainless steel, top unloading. Tank cars, as well as trucks, are pressurized with nitrogen gas at loading time to prevent oxygen contact as a result of temperature changes in transit. For customers utilizing only small quantities, VDC is packaged by Sigma Aldrich into Mini Bulk™ Returnable Containers. These are stainless steel, pressure rated, which minimize potential for exposure to humans or the environment. The volume packaged in these containers represents a very small percentage of the total production volume.

3.2 Volume

Non-confidential estimates of production capacity for VDC are difficult to obtain due to the limited number of global producers and the fact that The Dow Chemical Company is the only U.S. producer. PPG Industries, the other historical U.S. producer, closed its facility in 2000. Estimated U.S. demand for VDC was 150 million pounds in 1987 and was projected to rise to 170 million pounds in 1992. (Reed, 1993) The current and future demand has been impacted by the imminent phase-out of HCFC 141b, which had used significant quantities VDC as a feedstock in one of the commercial routes.

Reference:

Reed DJ; Kirk-Othmer Encyclopedia of Chemical Technology, 4th edition.5: 1017-1028 (1993).

3.3 Physical / Chemical Properties

Property	Value
Molecular Weight	96.94
Odor	Sweet
Appearance	Clear, Colorless Liquid
Density	10.1 lb/gal @ 20° C
Solubility in water, weight %	0.25 @ 25° C
Boiling point	31.7°C 760mmHg
Vapor Pressure	498 mm Hg @ 20° C
Flash Point	-19°F (Tag Closed Cup)
Flammable Limits in air (ambient conditions), vol. %	6.5 – 15.5
Reactivity	Air, water, sunlight, strong bases, aluminum, copper and its alloys

In the presence of oxygen, VDC forms a complex peroxide compound at temperatures as low as -40°C . This peroxide compound is unstable and shock-sensitive when dry. Inhibitor systems are added to delay peroxide formation but will not prevent it if the monomer is exposed to oxygen over an extended period of time.

These physicochemical properties have limited the use of VDC to closed-system applications.

3.4 Product Stewardship Program

There are multiple components to The Dow Chemical Company's product stewardship program for VDC. The key to all product stewardship efforts is to ensure that the user is as knowledgeable as Dow about the known human and environmental hazards and methods to handle the product in a safe and environmentally sound manner. A critical component of the program is the availability of product stewardship information. For VDC, this includes the product label, material safety data sheet, and VDC Safe Handling Guide. This guide outlines the known human and environmental hazards, first aid measures, safe handling practices, personal protective equipment use and procedures for unloading and storage.

In addition to providing product stewardship information, due to the physical and chemical hazards of VDC, an active customer assessment program is in place. The product steward, prior to first shipment, must approve all new applications and customer sites. If it is determined that the exposure to VDC can be managed both during processing and use, the product steward will approve the application. However, prior to first shipment, the product steward will provide on-site training on storage, safe handling and use, and consult on protective equipment and vapor monitoring methods, while reviewing the customer's operating discipline and status of their facilities. Recommendations are made on improvement opportunities and a customer response is required. If there is concern about whether VDC exposure can be controlled at a potential site and/or the capability of personnel to handle VDC safely, sales to a potential customer may be delayed or not approved. These customer assessments are updated at least every three years.

Another aspect of the VDC product stewardship program focuses on the distribution of VDC. Every three years, the business conducts a review of the potential risk associated with distribution of VDC. This includes a review of loading and unloading equipment, transportation routes, carrier performance, regulations, toxicity profile and the management plans in place to minimize the risks. This information is being provided on

the VDC product stewardship program to exhibit the program that has been developed to minimize the potential for exposure during its distribution and use.

3.5 Regulatory Limits, Listings and Approvals

While VDC has hazards, which have led to its inclusion in the various regulations outlined below, these regulatory requirements, impacting production, distribution, processing, use and disposal, have led to appropriate controls on exposure.

The following Regulatory listing / limits have been established for VDC:

Hazardous Air Pollutant under CAA Sec. 112

SOCMI Intermediate under CAA Sec. 111

Hazardous Organic NESHAP (HON) Synthetic Organic Chemicals (Sec. 111)

Clean Water Act Sec. 304(a)(1) Ambient Water Quality Criteria

Clean Water Act Sec. 307(a)(1) Toxic Pollutants

CERCLA 311 Hazardous Chemicals: RQ Code is B; RQ is 100lbs

RCRA Hazardous Constituent (waste codes:K073, 019,020,029 & F024,25,039)

RCRA Treatment Standards: wastewater std 0.025mg/L; Nonwastewater standard is 6.0 mg/kg

RCRA U List of Hazardous Wastes

Safe Drinking Water Act: mcl: 0.007mg/L; mclg: 0.007 mg/l

IARC Category: 3 – Unclassifiable or Probably Non Carcinogenic Agent

Clean Air Act Sec. 112: Regulated Flammable Substance;Threshold Quantity:10,000 lbs

DOT Marine Pollutant

International Marine Pollutant – Flammable Liquid, Corrosive, N.O.S.

ACGIH: TLV (8-hour) – 5 ppm; Carcinogen Category: A4

The following Regulatory Approvals for use in food applications have been established for VDC containing compounds:

The United States Food and Drug Administration (FDA) has approved the use of VDC based polymers for food contact use since the existence of such approvals.

Summarized below are the major approval categories granted by the FDA under 21 Code of Federal Regulations (CFR).

VINLYIDENE CHLORIDE

- Cleared for use in homo- and copolymer formation under 21 CFR 175.105 (adhesives)
- Cleared for use in the production of acrylic copolymers and vinyl acetate copolymers under 21 CFR 176.170 (Components of paper and paperboard in contact with aqueous and fatty foods).
- Cleared for use in polymer formation under 21 CFR 177.1010 (Semi-rigid and rigid acrylic and modified acrylic plastics)
- Cleared under 21 CFR 178.3790 (Acrylic polymer modifiers in semi-rigid and rigid polyvinyl chloride plastics)

VINYLLIDENE CHLORIDE (POLYMERIZED)

- Granted prior sanction for use and listed 21 CFR 181.30 (Substances used in the manufacture of paper and paperboard products used in food packaging)
- Cleared for copolymerization with vinyl chloride under 21 CFR 175.300 (Resinous and polymeric coatings), 21 CFR 175.380; 175.390 and 177.1210.
- VDC copolymerized is cleared for use in the food-contact surface of resinous and polymeric coatings under 21 CFR 175.320 (Resinous and polymeric coatings for polyolefin films)

- Cleared under 21 CFR 176.170 (Components of paper and paperboard in contact with aqueous and fatty foods) and 21 CFR 176.180 (Components of paper and paperboard in contact with dry food).
- Polymers, homopolymers and copolymers of VDC are cleared for use as the basic polymer under 21CFR 176.180 (components of paper and paperboard in contact with dry food).
- VDC copolymerized is cleared for use under 21 CFR 177.1200 (cellophane), 21 CFR 177.1400 (water-insoluble hydroxyethyl cellulose film); and as a coating under 21 CFR 177.130 (polyethylene terephthalate film).

Vinyl Chloride – VDC Copolymer Coatings – 21 CFR 172.210

Vinyl Chloride – VDC-2,3-Epoxypropyl Methacrylate Copolymers - 21 CFR 175.300; 175.380; 175.390, and 177.1210

VDC Copolymer Coatings – 21 CFR 179.45 (Packing materials for use during irradiation of prepackaged foods)

VDC Copolymer Coatings for Nylon Film – 21 CFR 175.360

VDC Copolymer Coatings for Polycarbonate Films – 21 CFR 175.365

VDC-Methacrylate Decyloctyl Copolymer

Cleared as the basic polymer under 21 CFR 177.1200 and 177.1400

4. Potential VDC Sources to Humans & Environment

The potential sources of VDC exposure to children and the environment could come from production, processing, use and disposal of VDC itself or through the degradation of higher chlorinated compounds already present in the environment. The following industrial processes have been identified as potential sources of VDC emissions: VDC production, VDC polymerization, use of VDC in specialty chemical production, VDC copolymer fabrication, and volatilization from waste treatment storage, and disposal. (Pacific Environmental Services, 1987) VDC is also a product of hydrolysis of 1,1,1-Trichloroethane and, to a lesser extent, through anaerobic degradation of trichloroethylene. Thus, VDC may be formed in landfills or in groundwater contaminated with 1,1,1-trichloroethane or trichloroethylene.

Reference:

Pacific Environmental Services, Toxic Air Pollutant/Source Crosswalk - A screening tool for locating possible sources emitting toxic air pollutants, EPA-450.4-87-023a.

4.1 VDC Manufacturing & Processing

During the manufacturing, processing and product transfer, the potential exists for small amounts of VDC to be released resulting in potential exposure to workers and the environment. Due hazards of VDC, numerous steps are taken to prevent its release. Releases can occur in the form of point source and fugitive emissions to air, land and water. In Section 4.1.1, the most recent U.S. EPA Toxics Release Inventory Report has been included, which outlines the reported releases from U.S. production and processing sites in 2000. In Section 4.1.2, the potential for occupational exposure is summarized.

4.1.1 U.S. Toxics Release Inventory

According to the 2000 Toxics Release Inventory (TRI), an estimate of 147,528 pounds of VDC were released to the environment, of which 98.7% was released into the atmosphere (USEPA, 2002). Since 1991, there has been a 49% reduction in TRI releases of VDC. A summary table, 4.1.1.1, outlining the 2000 releases recorded in TRI is included on the following page.

Table 4.1.1.1 United States EPA Toxics Release Inventory Releases – 2000

Row #	Facility	City	State	Total Air Emissions	Surface Water Discharges	Underground Injection	Releases to Land	Total On-site Releases	Total Off-site Releases	Total On- and Off-site Releases
1	W. R. GRACE & CO. CONN.	OWENSBORO	KY	68235	.	.	.	68235	.	68235
2	MORTON INTL. INC.	RINGWOOD	IL	33216	0	.	.	33216	.	33216
3	DOW CHEMICAL CO. MIDLAND OPS.	MIDLAND	MI	20895	3	.	0	20898	.	20898
4	SOLUTIA INC.	DECATUR	AL	7700	.	.	.	7700	.	7700
5	DOW CHEMICAL CO. FREEPORT	FREEPORT	TX	3710	0	.	0	3710	.	3710
6	PPG INDS. INC.	LAKE CHARLES	LA	2960	0	.	.	2960	.	2960
7	3M	DECATUR	AL	2750	.	.	0	2750	.	2750
8	DU PONT CHAMBERS WORKS	DEEPWATER	NJ	321	1620	.	36	1977	.	1977
9	APPLIED EXTRUSION TECHS. INC.	COVINGTON	VA	1645	1	.	.	1646	.	1646
10	VULCAN CHEMICALS	WICHITA	KS	1171	.	199	.	1370	.	1370
11	BORDEN CHEMICALS & PLASTICS OPERATING L.P.	GEISMAR	LA	1061	0	0	.	1061	.	1061
12	BAYER CORP.	SOUTH CHARLESTON	WV	934	0	.	.	934	.	934
13	LAROCHE INDS. INC. GRAMERCY FACILITY	GRAMERCY	LA	318	0	.	.	318	.	318
14	BFGOODRICH CO. LOUISVILLE PLANT	LOUISVILLE	KY	227	.	.	.	227	.	227
15	EASTMAN KODAK CO. KODAK PARK	ROCHESTER	NY	182	.	.	0	182	0	182
16	DOW CHEMICAL CO. DALTON PLANT	DALTON	GA	175	.	.	.	175	.	175
17	VULCAN MATERIALS CO. CHEMICALS DIV.	GEISMAR	LA	101	0	.	.	101	.	101
18	GEORGIA GULF CHEMICALS & VINYL L.L.C.	PLAQUEMINE	LA	44	0	.	.	44	7	51
19	BFGOODRICH PERFORMANCE MATERIALS	GASTONIA	NC	10	.	.	.	10	.	10
20	DOW CHEMICAL CO. LOUISIANA DIV.	PLAQUEMINE	LA	5	0	.	.	5	.	5
21	OCCIDENTAL CHEMICAL CORP.	GREGORY	TX	2	0	.	.	2	.	2
22	KODAK COLORADO DIV.	WINDSOR	CO	0
23	OXY VINYL L.P. LA PORTE VCM PLANT	LA PORTE	TX	0	0	.	.	0	.	0
24	OXY VINYL L.P. DEER PARK VCM PLANT	DEER PARK	TX	0	.	.	.	0	.	0
	Total			145662	1624	199	36	147521	7	147528

A correlation of data from the EPA Air Toxics Emissions Inventory with industrial source categories (SIC codes) shows that emissions of VDC are associated with coated fabrics and finishing plants, plastic materials and resins, synthetic rubber and fibers, industrial organic chemicals, photographic equipment and supplies, and sanitary services.

As these releases directly impact ambient air values, this information is included in the Ambient Air Exposure Assessment (5.2.1). The assessment primarily utilizes the U.S. EPA Air Toxics Data Archive, as it includes sources not represented by TRI, but the assessment also takes in consideration the TRI data.

References:

USEPA. Toxics Release Inventory Data Base. (2002)

4.1.2 Occupational

NIOSH (NOES Survey 1082 –1983) estimated that 2,675 workers were exposed to VDC in the United States (NIOSH, 1989). More recent estimates conducted by industry in the late 1990's suggest that the number of workers potentially exposed to VDC was less

than half of the 1980 estimate. This would include all operators, unloaders, maintenance workers, researchers, and anyone else who might handle or work with VDC. The reduction in workers could be due to a reduction in VDC consumption, increased VDC substitution as well as worker productivity improvements.

In a 1983 EPA Health Assessment Document, VDC concentrations in monomer and polymer manufacturing plants were reported to be 90-100ug/m³ (22-25 ppb) and 25-50 ug/m³ (6.2 and 12 ppb), respectively (U.S. EPA, 1985). Levels as high as 7,700 mg/m³ (1900ppm) were found in a VDC-ethyl acrylate copolymer monofilament fiber production plant. The estimated TWA exposure levels for different job categories in this same plant ranged from 6 to 70 ppm. More recent industry data suggests that 8-hour TWA exposure levels in monomer and polymer manufacturing plants have been reduced. The levels ranged from N.D. (0.02 ppm detection limit) to 3 ppm. There were values as high as 100 ppm reported during specific tasks, which were very short in duration and conducted infrequently. In these cases, where the potential for VDC exposure existed, respiratory protection, in the form of an approved, air-purifying, cartridge respirators or positive pressure, self-contained breathing apparatus was worn. The greatest potential for ambient air concentrations to exceed the ACGIH TLV of 5 ppm exist during transfer operations, sampling and maintenance activities (Dow, 2002). During such activities, respiratory protection would be worn.

References:

NIOSH. National Institute for Occupational Safety and Health. National Occupational Exposure Survey (NOES), Computer printout. (March 29, 1989)

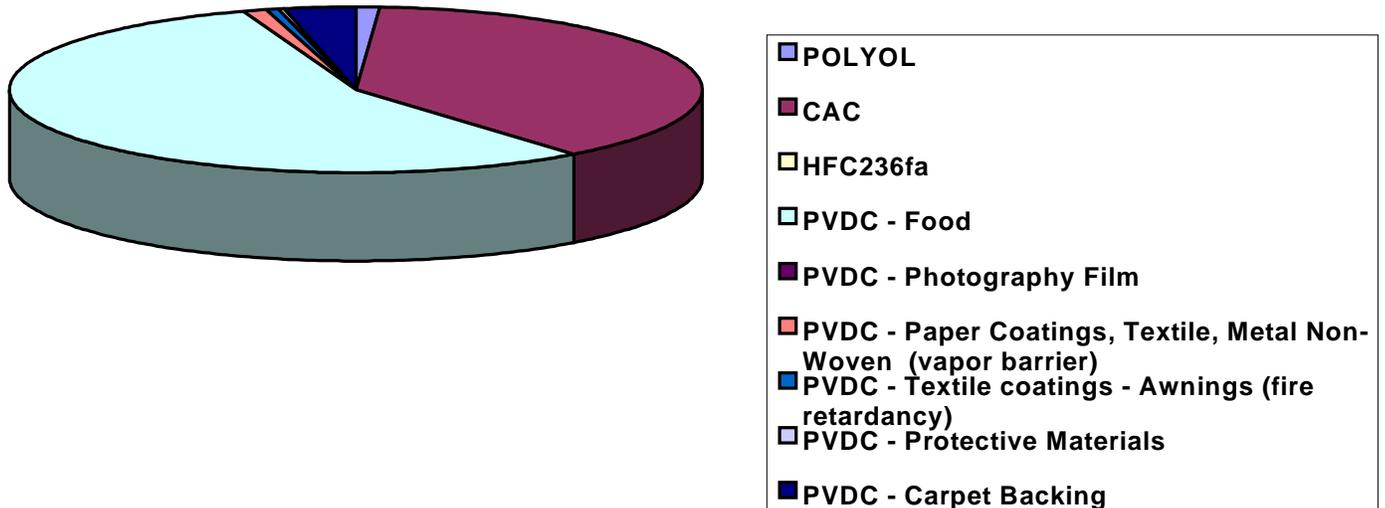
U.S. EPA ; Health Assessment document for vinylidene chloride. EPA-600/8-83-031F, Office of Health and Environmental Assessment, Washington, DC (1985)

Dow, unpublished data, (2002)

4.2 VDC Applications

VDC is produced solely for use as a chemical intermediate primarily in the production of polyvinylidene polymers, copolymer and terpolymers. Another key application is in the production of chloroacetyl chloride. It is also used in the production of a hydro-fluorocarbon. The pie chart below, illustrates the relative percentage of VDC utilized in the various applications for 2001.

2001 U.S. VDC Applications - Volume Distribution



Specific end-use application data is considered proprietary information by Dow and the VDC users due to the fact that there is a single U.S. producer, no importers and a limited number of VDC users.

To ensure that careful consideration was given to the relevance of each of the applications to children, each VDC customer was contacted to confirm exactly how the VDC was utilized and identify any potential for such exposure. Details about each of the applications are summarized below.

4.2.1 Polyvinylidene Chloride (PVDC) Applications

VDC can be reacted to produce both PVDC latex and resin polymers. It is typically produced either as a copolymer or terpolymer. Common monomers utilized in co- or terpolymers of VDC include vinyl chloride, acrylic esters such as methyl acrylate and acrylonitrile, and fluorinated compounds.

VDC copolymers can be divided into two groups: High-VDC copolymers (79 to 90%) used to form moisture and vapour barrier coatings and films; and low-VDC copolymers (10 to 70%) where VDC is mainly added to improve flame retardant and ignition resistance properties.

VDC-containing polymers are produced as emulsion polymers, as solvent-soluble powders for coating applications and as resins for extrusion and coextrusion.

PVDC Latex for Carpet Backing

Description: PVDC-containing latex is utilized in carpet backing to hold the yarn onto the backing, to hold individual fibers together and to adhere the secondary backing onto the yarn to deter delamination. Further, the latex is utilized to improve the ignition resistant properties of the fiber. It is only utilized in specialized carpet backings where the PVDC properties are valued. The majority of the carpet with PVDC-containing carpet backing is used in commercial operations, such as airports and hotels.

VDC Residual: The typical monomer residual level in this latex is extremely low, <5 ppm. This concentration is further reduced in the processing of the latex onto the carpet.

Relevance of Application to Children & Prospective Parents: Due to the use of this product in commercial operations, which could include child day care, the potential opportunity for exposure to children can not be excluded. However, the location of the VDC coating as well as the low level of residual in the latex makes exposure unlikely. A more detailed assessment of this potential exposure is included in Section 5.4.2.

VDC-based latex for Foil Scrim Kraft

Description: VDC-based latex is an adhesive formulation in the manufacture of Foil Scrim Kraft (FSK). FSK is a multi-layer product consisting of aluminum foil, fiberglass scrim and kraft paper. The VDC-based latex adhesive is used to laminate these three components together. FSK laminates are used as vapor barriers in the construction of industrial insulation where flame retardant properties are critical. It may also be used in commercial construction.

VDC Residual: The concentration of VDC residual in the latex is extremely low, less than 3 ppm.

Relevance of Application to Children & Prospective Parents: As this product is primarily used in industrial applications, this application is inconsequential to children. For others, when used in any application, the FSK product would be covered by other layer(s) of building material(s) preventing any potential exposure to VDC.

VDC-containing Latex for Photographic Film Coating

Description: VDC-containing latex is used as one of the coatings in certain types of specialty photographic film and paper. This latex layer has a different polymer overcoat.

VDC Residual: The level of VDC residual is known to be less than 0.1% in the latex and less than 0.001% in the final product.

Relevance of Application to Children & Prospective Parents :

Considering that the VDC-containing latex is covered with a polymer overcoat and that the use conditions do not support the migration of VDC from the inner layer, the trace levels of VDC should not be available for human exposure.

PVDC for Flame Retardant Fibers for Clothing

Description: PVDC is incorporated as a coating onto fibers to provide ignition resistance to clothing. It is typically used in articles of clothing used in industrial settings. It is not the common polymer coating used in children's clothing.

VDC Residual: The level of VDC residual in the application is < 5 ppm in the PVDC coating. The coating is applied to the fiber at a concentration of 1%.

Relevance of Application to Children & Prospective Parents: Considering the minor amount of coating that is applied to the fiber, as well as the potential for the VDC to be driven off during the high-temperature processing of the fibers, it has been determined that there is no potential for VDC to be present in the clothing.

PVDC for Food Packaging

Description: PVDC is selected for use with foods because of its excellent oxygen barrier capacity. For this application, PVDC is produced either as a solvent grade powder or resin or as a water-based dispersion. In either case, it is manufactured as a copolymer or terpolymer with various other monomer(s), depending upon the attributes needed for the application. The properties of PVDC do not support its use as a homopolymer in these applications. The majority of the PVDC copolymer/terpolymer used in food applications is a part of a multi-layered system, where the VDC-containing polymer is sandwiched between other films. In cases where it is produced as latex, the VDC-containing latex is dried to a powder and sprayed onto another polymer film. The copolymer emulsion can also be a component of a paper coating system to impart an oxygen and moisture barrier.

VDC Residual: Based on information received from various PVDC producers, the level of VDC residual in the PVDC is extremely low, ranging from 5 ppm to non-detect (1ppm).

Relevance of Application to Children & Prospective Parents: The use of VDC in products that have food contact does offer the potential opportunity for exposure. However, the conditions required for the VDC to migrate from the film as well as the low level of residual makes exposure unlikely. A more detailed assessment of this potential exposure is included in Section 5.4.1.

PVDC/Fluorinated Copolymer Application on Textiles

Description: VDC is used as a monomer in the manufacture of some fluorinated polymer products. These products are polymers in water emulsions or solutions. They are applied to selected textile fabrics to impart water and oil resistance properties. These fabrics are not used in children's clothing.

VDC Residual: Product analyses confirm that these polymers contain only residual quantities of unreacted VDC (less than 0.1%) if present at all.

Relevance of Application to Children & Prospective Parents: Based upon knowledge of the physical/chemical properties of VDC and knowledge of the textile processing conditions required to apply these polymers to the fabrics, there is no reasonable mechanism for VDC to be present on finished garments as a result of being treated with the VDC containing polymer.

4.2.2 Intermediate Applications

Chloroacetyl Chloride (CAC) Production:

Description: VDC can be used in the production of CAC by reaction with oxygen. The CAC is then utilized as an intermediate in the production of agricultural and pharmaceutical products.

VDC Residual: CAC contains no detectable levels of VDC.

Relevance of Application to Children & Prospective Parents: As the final products are several steps downstream from VDC and VDC is not detectable in CAC, it is also not detectable in the end-use product. Thus, there is not potential for exposure.

Urethane Foam Production:

Description: VDC is used as a component for a compound used in the production of automotive interior foam.

VDC Residual: Analyses confirm that there is less than 1ppm present in the component used in the production of foam.

Relevance of Application to Children & Prospective Parents: As this compound is further reacted prior to use, considering the processing conditions, there is essentially no potential for VDC exposure through such use.

HFC 236fa Production:

Description: VDC is used in the production of a chemical intermediate, which ultimately is converted to HFC 236fa for use in fire extinguishers.

VDC Residual / Relevance of Application to Children & Prospective Parents : As the HFC is several steps removed from the use of VDC, there is no detectable VDC residual in the final HFC product. Thus, there is no potential for exposure.

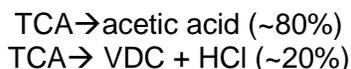
After reviewing each VDC application and its potential exposure to children and prospective parents, a determination was made on applications requiring further assessment. The use of VDC in PVDC latex for carpet backing and in PVDC for food packaging were selected for further exposure assessment due, primarily, to the potential for exposure to children and prospective parents.

4.3 Higher Chlorinated Products Degradation

VDC may be created in the environment as the result of degradation of higher chlorinated organic compounds. The fate of 1,1,1-trichloroethane (TCA) in groundwater and soil environments is governed by biotic and abiotic transformations. TCA is capable of undergoing biological reductive dechlorination to 1,1-dichloroethane (DCA) and then to chloroethane (CA), according to the following pathway (Vogel and McCarty, 1987; Klecka et al., 1990):



An alternative (abiotic) pathway for the destruction of TCA is achieved by elimination to 1,1-DCE and hydrolysis to acetic acid via the pathways shown below (Haag and Mill, 1988; and Vogel and McCarty, 1987):



The half-life for TCA via elimination to VDC is approximately two years.

The formation of VDC can also occur as the result of biotransformation of chlorinated ethenes, specifically perchloroethene (PCE) and trichloroethene (TCE). The biologically mediated reductive dechlorination reaction proceeds by sequentially removing chlorine atoms from the parent molecule, resulting in the formation of lesser-chlorinated ethene homologs. This process has the potential to result in the formation of dichloroethenes (DCE) with subsequent transformation to vinyl chloride and ethene (Wilson et al., 1986; Barrio-Lage et al., 1986). However, the biological transformation of TCE to DCE typically results in the formation of cis-1,2-DCE (>99%), with only small amounts of trans-1,2-DCE and VDC being formed. This transformation pathway is defined below:



VDC is also produced by the thermal decomposition of 1,1,1-TCA or 1,1,2-TCA and may therefore be emitted by burning waste solvents (Glisson, 1986). However, there is no evidence that higher chlorinated compounds (e.g. PCE and TCA) are capable of being transformed to VDC in the atmosphere.

4.3.1 Fate of 1,1-DCE in groundwater and soil

Biodegradation of VDC has been observed in both aerobic and anaerobic groundwater and soils. Biodegradation half-life ranges from 108 days in anaerobic aquifer sediments (McCarty et al., 1986) to 180 days in an aerobic surface soil (Klier et al., 1999). Loss of 1,1-DCE in groundwater and soil due to hydrolysis is not likely since the estimated hydrolysis half-life for VDC is 1.2×10^8 years (Jeffers et al., 1989).

4.3.2 Fate of VDC in air

Based on its physical-chemical properties – high vapor pressure and low water solubility – VDC is expected to exist primarily in the atmosphere as compared to other environmental compartments. VDC has an atmospheric oxidation half-life of two days due to attack by hydroxyl radicals (WHO, 1990). The major products from this reaction are formaldehyde, phosgene, and hydroxyacetyl chloride. Photooxidation of VDC in the presence of nitrogen dioxide and air yields phosgene, chloroacetyl chloride, formic acid, hydrochloric acid, carbon monoxide, formaldehyde, and ozone (Gay et al., 1976). The tropospheric lifetime of VDC under such conditions is estimated to be less than two days.

4.3.3 Summary

VDC is a chlorinated organic compound found in relatively low concentrations in air, groundwater, surface soils, and aquifer sediments. Sources of VDC include incidental release from manufacturing operations, conversion of 1,1,1-TCA to VDC via elimination, and bacterial conversion of PCE/TCE to VDC (minor). In groundwater and soil, VDC can be reductively dechlorinated to vinyl chloride and ethene under anaerobic conditions. Under aerobic conditions, VDC is likely used as a sole carbon source by microbes and is mineralized to CO₂. Atmospheric VDC is rapidly degraded (oxidized) in the presence of hydroxyl radicals. (Witt, M., 2002)

References:

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4.4. Summary of Potential VDC Sources

The potential for exposure to VDC has been well characterized. This review includes analyses of the VDC life cycle and customer surveys. A clear picture of potential exposure of humans, and in particular children, to VDC has emerged. Potential sources of exposure are limited and emissions are expected to continue to decline as they have for a number of years. At the present time, VDC is produced solely for use as a chemical intermediate. Applications are largely industrial-based "closed systems" polymer production operations. There is extremely limited potential for consumer exposure since only very low levels of VDC remain in the polymers. One of the greatest potential environmental sources of VDC is via the degradation of 1,1,1-trichloroethane. However, 1,1,1-trichloroethane has been phased out of production under the Montreal Protocol so the levels of VDC in the environment from this source are expected to continue to decline. Evidence of this decline can be seen in the ambient air and water data utilized in the exposure assessments.

5. Exposure Assessment

5.1 Exposure Pathways

5.1.1 Plausible Exposure Pathways

Based upon the usage profile and the physicochemical properties of VDC, the following pathways are considered by Dow to be the most plausible:

- (1) Inhalation of ambient air due to air emissions from manufacturing and processing facilities.
- (2) Inhalation of residential indoor air, due its presence in VDC containing latex that is used in the carpet backing, it being a volatile chemical, and its presence (although infrequently and low levels) in the TEAM study.

- (3) Ingestion of food that has been in contact with VDC containing polymer food wrap.
- (4) Ingestion of water due to its detection in groundwater and drinking water sources. (VDC's presence is a result of the degradation of higher chlorinated organic hydrocarbons.)
- (5) Dermal contact with carpet, due its presence in PVDC containing latex that is used in the carpet backing and because children are known to vigorously play on carpets.
- (6) Dermal contact with industrial insulation adhesive that uses VDC- containing latex.
- (7) Dermal contact with photographic film/paper that contains an inner layer of VDC-containing latex coating.
- (8) Dermal exposure to textiles, with VDC-containing polymer coating
- (9) Inhalation of fugitive air emissions in the workplace which may be generated during the production or processing of VDC.
- (10) Dermal contact of VDC releases in the workplace which may be occur during the production or processing of VDC.

Consumer applications where VDC is utilized as an intermediate with the final product several steps removed from the consumer were not considered to be plausible exposure pathways. Acute exposures were also not considered because the only potential exposure is to trace levels of VDC, which would not be acutely toxic.

5.1.2 Selected Exposure Pathways

Pathways of potential exposure to children and prospective parents were selected by considering physicochemical, usage and hazard data. Using such information, we have selected the first four pathways described in Section 5.1.1 above as those representing the greatest potential for exposure. The supporting data and exposure scenarios are described in the remainder of this Exposure Assessment Section.

The reason for not selecting the following six pathways for further assessment are denoted below:

- (1) Dermal contact with carpet, due its presence in PVDC containing latex that is used in the carpet backing and because children, particularly infants, are known to vigorously play on carpets.

Reason: Determination was made to consider exposure via inhalation of indoor air rather than dermal contact as the inhalation exposure was viewed to be a worst case scenario. Thus, the dermal contact scenario was removed from consideration by Dow for further assessment.

- (2) Dermal contact with industrial insulation adhesive that uses VDC- containing latex
Reason: FSK is used primarily in industrial settings thus the exposure is considered inconsequential to children. For prospective parents, dermal exposure to VDC is highly unlikely as the residual level in the latex is extremely low and the insulation would be covered by other layer(s) of building material(s). Further, the assessment of the hazard data indicates that there is no indication that VDC is associated with reproductive or developmental toxicity. VDC has also not been found in breast milk. Thus, this scenario was removed from consideration for further assessment.

- (3) Dermal contact with photographic film/paper that contains an inner layer of VDC-containing latex coating

Reason: The VDC containing latex is utilized in an inner layer of the film, paper with essentially no potential for migration. Further, the assessment of the hazard data indicates that there is no indication that VDC is associated with reproductive or developmental toxicity. VDC has also not been found in breast milk. The application is considered irrelevant to children and prospective parents. This exposure scenario was removed from consideration for further assessment.

(4) Dermal exposure to textiles, with VDC-containing polymer coating

Reason: Based upon knowledge of the physical/chemical properties of VDC and knowledge of the textile processing conditions required to apply these polymers to the fabrics, there is no reasonable mechanism for VDC to be present on finished garments as a result of being treated with the VDC containing polymer. Further, the assessment of the hazard data indicates that there is no indication that VDC is associated with reproductive or developmental toxicity. VDC has also not been found in breast milk. Thus, the application is inconsequential to children and prospective parents. The scenario was removed by Dow from consideration for further assessment.

(5) Inhalation of fugitive air emissions in the workplace which may be generated during the production or processing of VDC.

Reason: There is minimal potential for VDC exposure to occur in the workplace as it is produced and processed in closed systems. This is supported by the industrial hygiene data collected in numerous workplaces of various types. When the potential for exposure is greater, i.e. during maintenance of vessels or piping, personal protective equipment such as positive pressure, self-contained breathing apparatus is worn. Additionally, the assessment of the hazard data indicates that there is no indication that VDC is associated with reproductive or developmental toxicity. VDC has also not been found in breast milk. Thus, this occupational exposure scenario was removed from consideration for further assessment.

(6) Dermal contact of VDC releases in the workplace which may occur during the production or processing of VDC.

Reason: There is minimal potential for VDC exposure to occur in the workplace as it is produced and processed in closed systems. This is supported by the industrial hygiene data collected in numerous workplaces of various types. Additionally, due to the physical form of VDC during production and processing, it is highly unlikely for dermal exposure to occur. In the rare event that potential for dermal contact exists, personnel wear premeation-resistant clothing and positive pressure, self-contained breathing apparatus. Further, the assessment of the hazard data indicates that there is no indication that VDC is associated with reproductive or developmental toxicity. VDC has also not been found in breast milk. Thus, this occupational exposure scenario was removed from consideration for further assessment.

5.2 Ambient Air Exposure Assessment

5.2.1 Distribution of Exposure

A study has been conducted to provide estimates of the distribution of exposures for children in the United States due to inhalation of ambient air that may contain VDC. An estimate of the exposure distribution for the general public from this route is also provided. The distribution of ambient air concentrations is obtained from the air toxics data archive maintained through the cooperation of the USEPA and state air pollution control professionals. This database contains over 20,000 observations for VDC from 19 monitoring programs in many locations. Although detection limits are not available for these observations, about half of the positive detections are less than $0.1 \mu\text{g}/\text{m}^3$, indicating that methods with acceptably low detection limits were available during the

time samples were collected and analyzed. The relatively low percentage (10%) of detectable concentrations of VDC in this large number of observations suggests that measurable VDC exposure from inhalation of ambient air is likely to be an infrequent event for the typical person or child.

The quantitative estimates of VDC exposure via inhalation are made using the assumption that all inhaled air contains quantifiable VDC and that the distribution of VDC concentration in the air is equal to that of the positive detections reported in the database. The median (50%-tile) calculated exposures for childhood and lifetime exposure scenarios are 0.12 and 0.07 $\mu\text{g}/\text{kg}/\text{day}$, respectively. These are factors of 416 and 714 less than the health protective guidance level of 50 $\mu\text{g}/\text{kg}/\text{day}$. The maximum childhood exposure calculated in 100,000 simulations is 2.13 $\mu\text{g}/\text{kg}/\text{day}$, a factor of 23 less than the health protective benchmark. This is the one in 100,000 value and corresponds to the 99.999th %-tile of the childhood exposure distribution. The 99.999th %-tile lifetime exposure is 1.78 $\mu\text{g}/\text{kg}/\text{day}$, a factor of 28 less than the benchmark. The complete study has been included as Appendix A.

5.2.2 Summaries of Additional Relevant Air References

Although the following reference material is not explicitly used in the ambient air exposure assessment, it is generally consistent with the air toxics data archive used in that analysis. There are some higher reported air concentrations. These are from the late 1970's and early 1980's when 1,1,1-Trichloroethane (1,1,1-TCA) was a potential air contaminant and only for the studies that used high temperature thermal desorption. The higher temperature had the potential to convert 1,1,1-TCA to vinylidene chloride in the analytical procedure. The studies in the early 1980's that used lower temperature methods always had greater sensitivity and lower reported vinylidene chloride concentrations. Over 90% of the data in the air toxics data archive was obtained after 1990 when 1,1,1-TCA use was being reduced and eliminated. The air toxics data archive, which contains more recent data, is less likely to be confounded by the presence of 1,1,1-TCA.

The California REL is 70 $\mu\text{g}/\text{m}^3$, the USEPA IRIS RfC is 200 $\mu\text{g}/\text{m}^3$. These correspond to about 20 ppb and 50 ppb. Only a few data points in the tables below exceed these values. This is one entry of 76 $\mu\text{g}/\text{m}^3$ for ambient air, in Wallace et. al. 1982 and six values greater than 1000 $\mu\text{g}/\text{m}^3$, in Wallace et. al. 1991, measured in the early 1980's. The relevance of these values to this VDC assessment were discussed in detail in the review of the Biomonitoring data, section 2.2.1

1) Grimsrud EP, Rasmussen RA. Survey and Analysis of Halocarbons in the Atmosphere by Gas Chromatography-Mass Spectrometry. Atmos Environ 9:1014-1017. 1975.

High sensitivity (5 ppt detectable) and precision (± 5 per cent) are afforded by a direct linkage to the mass spectrometer of the entire gas chromatographic effluent. Sample volumes of 20 cm^3 are flushed onto chromatographic columns, which are temperature-programmed from -60°C to 100°C . Measurements were made in rural Pullman, Washington, from December 1974 to February 1975. The combined cis, trans, and 1,1, dichloroethylenes were nondetectable at a 5 ppt detection limit.

2) Singh, H.B., Seles, L.J., Stiles, R.E. Distribution of Selected Gaseous Organic Mutagens and Suspect Carcinogens in Ambient Air. Environmental Science and Technology 16 872-880. 1982.

1,1-Dichloroethylene (vinylidene chloride) was present at an average concentration of 0.01 – 0.03 ppb. However, it was below the detection limit of 5 ppt during 30-50% of the time at all sites.

VDC concentrations - ambient air:

Houston 15-24 May 1980

	Conc (ppt)	Conc ng/m ³
Mean	25	99
Max	136	
Min	<4	

St. Louis 30 May - 8 Jun 1980

	Conc (ppt)	Conc ng/m ³
Mean	9	36
Max	34	
Min	<4	

Denver 16-26 Jun 1980

	Conc (ppt)	Conc ng/m ³
Mean	31	123
Max	224	
Min	<4	

Riverside 2-12 July 1980

	Conc (ppt)	Conc ng/m ³
Mean	9	36
Max	56	
Min	<4	

Staten Island 27 Mar - 5 Apr 1981

	Conc (ppt)	Conc ng/m ³
Mean	(-)	(-)
Max	(-)	
Min	(-)	

Chicago 21-30 Apr 1981

	Conc (ppt)	Conc ng/m ³
Mean	22	87
Max	68	
Min	3	

Pittsburg 8-16 Apr 1981

	Conc (ppt)	Conc ng/m ³
Mean	(-)	(-)
Max	(-)	
Min	(-)	

3) Singh, H.B., Seles, L.J., Smith, A.J. and Shigeshi, H. Measurements of Some Potentially Hazardous Organic Chemicals in Urban Environments. Atmospheric Environment 15 601-612. 1981.

The primary means of analysis was gas chromatography. Cryogenic pre-concentration techniques at liquid-O₂ temperature were extensively employed. A typical ambient air sample was 500mL. No thermal desorption was observed from Tenax GC. VDC was always present at relatively low concentrations, and its measured concentration never exceeded 0.2 ppb. Average exposure at any of the sites did not exceed 3 µg/day. The low abundance of CH₂CCl₂ is at least in part due to the high reactivity of CH₂CCl₂. A 30% loss per day is estimated.

VDC Concentrations in Ambient Air

Los Angeles 9-21 Apr 1979

	Conc (ppt)
Mean	4.9
Max	9.7
Min	1

Phoenix 23-Apr - 6-May

	Conc (ppt)
Mean	29.8
Max	15.8
Min	<1

Oakland 28 Jun - 10 Jul 1979

	Conc (ppt)
Mean	12.6
Max	24.4
Min	4.8

The entries for the Phoenix location are faithfully copied from the author's table. It is clear that there is a typographical error in the Phoenix mean and maximum values, but nonetheless, the values are low.

4) Harkov, R., Kebbekus, B., Bozzelli, J., and Ling, P.J. Measurement of Selected Volatile Organic Compounds at Three Locations in New Jersey during the Summer Season. *Journal of the Air Pollution Control Association* 33 1177-1183. 1983.

Samples were thermally desorbed from the Tenax (250°C) and Spherocarb (350°C) traps into a 10 mL stainless steel cylinder fitted with a stainless steel bellows valve.

VDC concentrations in Urban air July 6 - Aug 16, 1981.

	Newark Conc (ppb)	Elizabeth Conc (ppb)	Camden Conc (ppb)
Mean	0.38	0.35	0.36
N	35	34	30

5) Harkov, R., Kebbekus, B., Bozzelli, JW, Lioy, PJ, and Daisey, J. Comparison of Selected Volatile Organic Compounds During the Summer and Winter at Urban Sites in New Jersey. *Science of the Total Env.* 38 (1984) 259-274.

Samples were thermally desorbed from the Tenax-GC (at 250°C) and Spherocarb (at 350°C) traps into an evacuated 10 mL stainless steel cylinder fitted with a stainless steel bellows valve.

VDC concentrations in Urban air July 6 - Aug 16, 1981.

	Newark Conc (ppb)	Elizabeth Conc (ppb)	Camden Conc (ppb)
Mean	0.38	0.35	0.36
N	35	34	30

VDC concentrations in Urban air Jan 18 to Feb 26, 1982.

	Newark Conc (ppb)	Elizabeth Conc (ppb)	Camden Conc (ppb)
Mean	0.31	0.52	1.02
N	23	29	31

6) Wallace, L., Zweidinger, R., Erickson, M., Cooper, S., Whittaker, D., Pellizzari, E. Monitoring Individual Exposure. Measurements of Volatile Organic Compounds in Breathing-Zone Air, Drinking Water, and Exhaled Breath. *Environment International* 8 269-282, 1982.

Estimated levels of selected vapor-phase organics in ambient air associated with human participants (Lamar University student study) ($\mu\text{g}/\text{m}^3$) – for Vinylidene Chloride												
Participant No.												
30001	30002	30003	30004	30005	30011	30012	30013	30014	30015	30016	LOD(a)	QL(b)
416	1.4	76	1	1.1	-	7	5.7	2.1	4.6	-	0.12	0.6

Estimated levels of selected vapor-phase organics in ambient air for several human subjects (University of North Carolina at Chapel Hill study) ($\mu\text{g}/\text{m}^3$) – for Vinylidene Chloride						
Participant Number						
40001	40002	40003	40011	40012	40013	
14	27	9.8	3.5	5.7	7	

Estimated levels of selected vapor phase organics in breath (Lamar University student study) ($\mu\text{g}/\text{m}^3$) -- for Vinylidene Chloride												
Participant No.												
30001	30002	30003	30004	30005	30011	30012	30013	30014	30015	30016	LOD	QL
15 ± 2.8	0.08	26 ± 8.0	0.08	2.9	0.08	0.08	0.5 T	5.8 ± 1.6	3.8 ± 1.2	0.08	0.16	0.82

Estimated levels of selected vapor phase organics in breath of human subjects (University of North Carolina at Chapel Hill study) ($\mu\text{g}/\text{m}^3$) -- for Vinylidene Chloride						
Participant Number						
40001	40002	40003	40011	40012	40013	
4.5 ± 0.39	14 ± 1.3	5.5 ± 1.3	3.9 ± 0.09	7.7 ± 0.05	7.9 ± 0.65	

(a) - Limit of Detection (LOD) was defined as $S/N = 4$ for m/z ion selected for quantification, all values given in $\mu\text{g}/\text{m}^3$

(b) - Quantifiable limit (QL) was defined as $5 \times \text{LOD}$ or $S/N = 20$, all values given in $\mu\text{g}/\text{m}^3$

T -trace amount

Table 3.1 Mean Concentration (ppb-V) (b)								
For the compound 1,1 Dichloroethylene							Range	Occurrence
Site 1	Site 3	Site 4	Site 7	Site 8	Site 11	Means	of Frequency (%) (c)	
<LLD	<0.5	<0.5	<0.5	<0.5	<0.5	<LLD - <0.5	4.50%	

(b): Six month (September 18, 1987 - March 16, 1988) arithmetic average for this site.

(c): Frequency of occurrence of the compound ($\#$ of observations * 100/ $\#$ of observations possible including all sites

LLD: Lower Limit of Detection

7) Wallace, L.A., Comparison of Risks from Outdoor and Indoor Exposure to Toxic Chemicals. Environmental Health Perspectives 95 7-13. 1991.

The limits of detection for VDC ranged from 3 to 14 $\mu\text{g}/\text{m}^3$, about an order of magnitude worse than for most of the other target VOC's. in the TEAM study. Out of 1085 personal air samples collected from 355 New Jersey residents over three different seasons, only 77 (7%) had measurable concentrations of VDC. (Another 107 (10%) showed trace concentrations.)

The population risk for such rarely detected chemicals can be calculated, but the interpretation of the risk presents difficulties.

Taken from Table 1.

Chemical	Exposure Concentration $\mu\text{g}/\text{m}^3$ ^a	Outdoor Air Concentration ^b $\mu\text{g}/\text{m}^3$
Vinylidene Chloride	6.5 ^d	<1

^a Arithmetic means based on a 24-hr average exposures of ~ 750 persons in 6 urban areas measured in the TEAM Studies.

^b Based on backyard measurements in 175 homes in six urban areas.

^d Six measurements exceeding 1000 $\mu\text{g}/\text{m}^3$ were dropped from the calculation; inclusion of the measurements leads to an average exposure of 150 $\mu\text{g}/\text{m}^3$.

8) Tetra Tech EM, Inc., Monthly Ambient Air Monitoring Reports, Freeport, TX. October 1997 – August 1998. Prepared for USEPA, Office of Solid Waste, Work Assignment No. R06080, Contract No. 68-W4-0007.

Of the 297 monitoring values collected from six locations around chemical manufacturing facilities in Freeport Texas, from October 1997 to August 1998, 247 (83%) are ND at a reliable detection limit of 0.13 ppbv (0.52 $\mu\text{g}/\text{m}^3$). Twenty four (8%) are between the RDL and 1 $\mu\text{g}/\text{m}^3$, and 24 (8%) are between 0.252 ppbv (1 $\mu\text{g}/\text{m}^3$) and 1.262 ppbv (5 $\mu\text{g}/\text{m}^3$). Two of the values (0.7% of the 297) are greater than 1.262 ppbv (5 $\mu\text{g}/\text{m}^3$).

Freeport Texas is the only US location of VDC production facilities and is the location of a large petrochemical complex.

9) Tetra Tech EM, Inc., Monthly Ambient Air Monitoring Reports, Geismar, LA. January 1998 – August 1998. Prepared for USEPA, Office of Solid Waste, Work Assignment No. R06080, Contract No. 68-W4-0007.

Only one of the 117 monitoring values (0.85%) collected from three locations around chemical manufacturing facilities in Geismar, Louisiana, from January 1998 to August 1998, exceeded the reliable detection limit, its concentration was 0.26 ppbv or 1.0 $\mu\text{g}/\text{m}^3$. Geismar is the home of a large petrochemical complex.

10) Air Toxics Data Archive – Air Toxics Monitoring Subcommittee – STAPPA/ALAPCO/USEPA, www.sdas.battelle.org/airtoxics/index.php, Feb 20, 2002.

Summary statistics are available on-line from the Internet for 21534 observations of VDC concentration in outdoor air. These are the 25th, 50th, and 75th percentiles for the distribution of observed concentrations in a given year in a given state, also included are the maximum and average values observed in a given year in a given state. The data are given as zero concentration when VDC was not detected. Detection limits were not given.

Only 8 of the 42 site-year maximum values exceed $1 \mu\text{g}/\text{m}^3$ and only one 75th percentile, the 1994 Indiana set of 38 observations, exceeded $1 \mu\text{g}/\text{m}^3$. Since a large number of observations, ca. 15k, are associated with a year and state having a maximum value in the tenths or hundredths of a $\mu\text{g}/\text{m}^3$ it can be concluded that the detection limit in these cases is even lower.

11) Pratt GC, Palmer K, Wu CY, Oliaei F, Hollerbach C, Fenske MJ. An Assessment of Air Toxics in Minnesota. *Environ Health Perspect* 108:815-825 (2000).

Air monitoring samples acquired from a statewide network of stations selected for three different programs, one to monitor air quality in Minneapolis-St. Paul, another to monitor specific sources and finally a third group of sites was established to provide a 1-year snapshot of concentrations at sites throughout the state. All samples were acquired in the 1990's with most samples collected from 1995-1999. Six sites were still active as of September 2000. The monitored air concentration values for a collection of VOC's and metals were compared to values calculated by air dispersion modeling in the USEPA Cumulative Exposure Project (CEP).

There were 3650 samples with analysis for VDC, of these 3261 (89%) were less than the lower limit of detection of $0.14 \mu\text{g}/\text{m}^3$. The maximum VDC concentration measured was $3.08 \mu\text{g}/\text{m}^3$.

5.3 Water Exposure Assessment

5.3.1 Distribution of Exposure

A study has been conducted to provide estimates of the distribution of exposures for children in the United States due to drinking water that may contain VDC. An estimate of the exposure distribution for the general public from this route is also provided. The distribution of water concentrations is obtained from the national contaminant occurrence database (NCOD) maintained by the USEPA. This database contains over 64,000 observations for VDC from more than 9,000 public water systems. The low percentage (1.5%) of VDC concentrations above the detection limit for this large number of observations and monitoring sites suggests that measurable VDC exposure from the ingestion of tap water is a very infrequent event for the typical person or child.

The quantitative estimates of VDC exposure via drinking water made using either screening or Monte Carlo techniques yield estimated exposures well below the $50 \mu\text{g}/\text{kg}/\text{day}$ RfD guidance level. The screening estimate of adult exposure, $0.009 \mu\text{g}/\text{kg}/\text{day}$, was identical to the estimate of median exposure obtained using Monte Carlo methods. The screening estimates for the children and teen typical exposures, 0.012 and $0.008 \mu\text{g}/\text{kg}/\text{day}$, are marginally greater than the $0.008 \mu\text{g}/\text{kg}/\text{day}$ median obtained for the 18 years of childhood using Monte Carlo methods. The complete study has been included as Appendix B.

5.3.2 Summaries of Additional Relevant References

Although the following reference material is not explicitly used in the water exposure assessment, it is consistent with the primary data used in that analysis.

1) Wallace, L.A., Pellizzari, E.D., Hartwell, T. D., Sparaciro, C., Whitmore, R., Sheldon, L., Zelon, H., Perritt, R. The TEAM Study: Personal Exposures to Toxic Substances in Air, Drinking Water, and Breath of 400 Residents of New Jersey, North Carolina, and North Dakota. *Env. Research* 43 290-307. 1987.

Each study participant collected two tap water samples. VDC concentrations were very low. Mean values were 0.2 ppt, 0.1 ppt, and 0.2 ppt, for New Jersey participants in the fall of 1981, summer of 1982 and winter of 1983, respectively. The corresponding maximum values were 2.4 ppt, 2.5 ppt, and 0.9 ppt, respectively.

2) Staples, CA, Werner A, Hoogheem T; Assessment of priority pollutant concentrations in the United States using STORET database. *Environ Toxicol Chem* 4:131-142 (1985).

This is an analysis of data in U.S. EPA's STORET database. Of 1350 effluent samples, 3.3% contained detectable VDC with a median concentration of less than 1 µg/L (ppb). Of 8714 ambient water samples, 6.0% contained detectable VDC with a median concentration of less than 0.1 µg/L.

3) Otson R., Williams RT, Bothwell PD. Volatile Organic Compounds in Water at Thirty Canadian Potable Water Treatment Facilities. *J. Assoc. Off. Anal. Chem.* 65 1370-1374 (1982).

VDC quantitation limits in water were between 5 and 10 micrograms/L. VDC was not detected in any raw water and in only one finished water sample.

4) Kaiser, KLE, Comba, ME, Huneault, H. Volatile Halocarbon Contaminants in the Niagara River and in Lake Ontario. *J. Great Lakes Res.* 9 212-233 (1983).

Water samples from 95 stations in Lake Ontario and 16 stations in the lower Niagara River were analyzed for volatile halocarbons and carbon disulfide. 1,1-dichloroethylene (VDC) was observed either at trace levels or absent at most stations. VDC was not detected at the 16 stations in the lower Niagara river and at 84 of the 95 stations in Lake Ontario, trace amounts were detected at six Lake Ontario stations, quantifiable amounts were detected at the remaining 5 Lake Ontario stations. The five quantifiable samples gave an arithmetic average of 0.8 ppb. The detection limit for VDC was 80 ng/L

5) Cole RH, Frederick RE, Healy RP, Rolan RG. Preliminary findings of the Priority Pollutant Monitoring Project of the Nationwide Urban Runoff Program. *J Water Pollut Control Fed* 56:898-908. 1984.

This program is designed to help determine which priority pollutants are in urban stormwater runoff, how frequently, and at what concentrations, as well as evaluate the potential impacts of priority pollutants from urban runoff on aquatic life and water supplies.

Samples were collected from 15 cities. VDC occurred in runoff water samples from one city, Eugene Oregon. Occurrence is given as 3%, this corresponds to around 3 of the 86 samples. The concentration range for these samples was 1.5 to 4 µg/L (ppb). Since VDC was rarely detected relative to some other analytes it was not selected for further analysis.

6) Lesage, S, Jackson, RE, Priddle, MW, and Riemann, PG. Occurrence and Fate of Organic Solvent Residues in Anoxic Groundwater at the Gloucester Landfill, Canada. *Env Sci and Technology* 24 559-566. (1990).

The disposal of organic chemicals in trenches at a waste disposal site near Ottawa, Ontario, Canada, has resulted in the contamination of the underlying aquifer. The

organic residues measured in groundwater samples are reported and mechanisms of contaminant transport in the aquifer discussed.

VDC was not detected in 57% of the samples; it was detected at 0.9 to 60 micg/L (ppb) in the remaining 43% of the 37 samples collected. It was noted that the presence and relative concentration of VDC was consistent with transformation of higher chlorinated compounds as a source.

5.4 Application Exposure Assessments

5.4.1 Food Wrap – Application Exposure Assessment

VDC copolymers are used in food wrap applications. These food wraps have the potential to contain residual VDC monomer. The purpose of this assessment is to evaluate the potential for exposure and subsequent risk from residuals that might be released from the film to wrapped food and then consumed. Estimates of both child and adult exposure are included. This study, included below, uses conservative, health protective assumptions to estimate exposure from the use of food wraps containing residual VDC.

Study Title: “Potential Oral Exposure to Vinylidene Chloride from the Use of Food Wrap” Regulation:

The Food and Drug Administration (FDA) regulates food contact materials in the United States. The FDA has issued recommendations for methods used to calculate and measure migration out of food contact material (FDA, 2002).

Exposure Scenario:

The potential oral exposure occurs from eating food that contains VDC monomer that has migrated out of food wrap. The variables that affect exposure include: the amount of food that is wrapped in the polymer film, the amount of film wrapping the food, the amount of the residual in the film, and the amount of the residual that migrates out of the film and into the food. The amount migrating out of the film will depend on contact time, temperature, and the physical and chemical properties of the food, the film, and the monomer.

Guidance Levels:

IRIS Oral RfD – 0.05 mg/kg/day (USEPA, 2002)

Draft IPCS Concise International Chemical Assessment Document – 1,1-Dichloroethene Tolerable Intake – 0.05 mg/kg/day (WHO, 2002)

Assumptions:

The estimate of daily intake is made using methods recommended by the FDA. The daily intake is the product of the total amount of diet consumed in a day (kg), the fraction of the diet that comes into contact with film (CF), and the concentration in food <M> that results from contacting the film. The concentration in food that results from contacting the film is based upon measurements of the amount of material migrating out of the film into the appropriate food simulant.

The amount of VDC that migrates out of a typical PVDC food wrap film has been measured using 200 square inches of food wrap in 200 mL of 212°F peanut oil for one hour (Lickly, 1988). The film had a measured residual VDC monomer content of 7 ppm. A typical current manufacturing specification for maximum residual VDC monomer in food wrap polymer is 5 ppm. Under these conditions the amount of VDC monomer migrating out of the film was less than the method quantitation limit of 50 ng VDC/mL of oil or 50 ng VDC/sq in of film. Using the standard FDA assumption that 10 grams of

food contact 1 sq. in. of film the upper limit on the amount of VDC migrating out of the film and into food is:

$$\langle M \rangle = (50 \text{ ng VDC/sq in film}) / (10 \text{ g food/sq in film}) = 5 \text{ ng VDC} / \text{g food.}$$

The FDA assigns polyVDC (PVDC) a consumption factor (CF) of 0.05. $CF = 0.05$

Calculation of Estimated Daily Intake (EDI):

The estimated daily intake is calculated as the product of the amount of food consumed in a day, the fraction of a person's diet that contacts the film containing the residual (CF), and the concentration in the food $\langle M \rangle$ that results from that contact. The FDA gives the equation,

$$EDI = \langle M \rangle \times CF \times 3 \text{ kg food (solid and liquid)/person/day.}$$

Substituting:

$$\langle M \rangle = 5 \text{ ng VDC} / \text{g food and}$$

$$CF = 0.05 \text{ gives}$$

$$EDI = 0.75 \text{ } \mu\text{g VDC/day.}$$

This is about 0.011 $\mu\text{g} / \text{kg/day}$ for a 70 kg adult. Assuming that a 20-kg child consumes the same 3 kg food/day gives 0.0375 $\mu\text{g} / \text{kg/day}$. These estimated daily intakes are 1300 to 4500 times lower than the guidance level of 0.05 mg/kg/day (50 $\mu\text{g} / \text{kg/day}$).

Summary:

The estimated daily intake of VDC is estimated as less than 0.011 $\mu\text{g} / \text{kg/day}$ for a 70-kg adult and less than 0.0375 $\mu\text{g} / \text{kg/day}$ for a 20 kg child. These are more than 3 orders of magnitude below the guidance levels set by regulatory authorities. These calculations provide overestimates of exposure to VDC monomer through the use of polyvinylidene chloride-containing food wrap. They are not estimates of the actual levels of exposure because the amount of VDC assumed to exist in the film is taken as the quantitation limit, the amount measured in the film was less than the quantitation limit. (Fontaine, D.D., 2002)

References:

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5.4.2 Carpet Latex – Application Exposure Assessment

Vinylidene chloride-containing polymers are components in some latex emulsions. These latex emulsions are used in carpet manufacturing and have the potential to contain residual VDC. This assessment evaluates the potential for inhalation exposure to residual VDC that might be released from the carpet. Estimates applicable to both child and adult exposure are included. This assessment, included below, uses conservative health protective assumptions to estimate exposure from carpet manufactured using a latex emulsion containing residual VDC.

Study Title: *“Potential Chronic Inhalation Exposure to Vinylidene Chloride from the Use of Latex Emulsion in Carpet Manufacture”*

First Inhalation Exposure Scenario:

Carpet covers all the floors in the living and working space.

The carpet is made using 20 ounces of wet latex per square yard of carpet. This is conservative. A more typical amount is 12 ounces of wet latex per square yard of carpet.

All the wet latex contains 3 ppm of residual VDC monomer.

No VDC is lost curing the latex during manufacturing. This is a health protective overly conservative estimate of the amount of residual monomer VDC in manufactured carpet.

No VDC is lost during storage, prior to installation of the carpet. This is a health protective overly conservative estimate of the amount of residual monomer VDC in installed carpet.

The carpeted room has a ventilation rate of 0.3 air changes per hour. Most annual average residential air exchange rates are greater than this value. (Murray and Burmaster 1995) The USEPA recommends using 0.45 air changes per hour as a typical residential ventilation rate in exposure calculations. (USEPA 1997)

The carpeted space has an eight-foot ceiling. Industry experts indicate that most carpet is not replaced with new carpet for at least five years. All the residual monomer VDC in the latex in the carpet is released during the five-year life of the carpet. This is a health protective overly conservative assessment.

Second Inhalation Exposure Scenario:

In this scenario the emission rate of VDC from carpet decreases as first-order decay. A constant fraction of the available VDC is lost in a given time period. Initially the concentration of VDC in the carpet is highest and the rate of release is fastest. Over time the amount available for release is reduced and the rate of release is reduced. Since the rate constant for the release is not precisely known, the release rate constant is assumed to correspond to a release half-life of 2 weeks, 1 year, or 5 years. All other assumptions are the same as for the first scenario.

These are conservative health protective scenarios because they overestimate the proportion of carpeted space and the proportion of carpet manufactured with latex that contains residual VDC. The estimated amounts of latex used in carpet and residual VDC in latex are greater than typical values. The result is an overly conservative estimate of the amount of VDC that migrates from the carpet into the room.

Inhalation Guidance Levels:

IRIS Inhalation RfC – 0.2 mg/m³ (200 µg/m³) (Integrated Risk Information System, 2002)

California Chronic Inhalation Reference Exposure Limit – 0.07 mg/m³ (70 µg/m³)

The USEPA and California guidance levels were obtained by applying health protective uncertainty factors (UF) to the no observed adverse effect level, NOAEL, or a benchmark concentration level, BMCL, for the most critical effect obtained from

inhalation tests with animals. Both agencies determined that liver toxicity was the critical effect.

The California guidance level is based on a 90-day continuous exposure experiment with Guinea pigs (Pendergast et al. 1967). The NOAEL for the critical effect was 20 mg/m³. Applying uncertainty factors of 10 for subchronic to chronic extrapolation, 10 for intraspecies variability, and 3 for interspecies variability gives a net uncertainty factor of 300. Dividing the NOAEL by the UF gives the chronic inhalation REL of 70 µg/m³.

The USEPA IRIS RfC is based upon an 18 month, 6 hour per day exposure using rats (Quast et al. 1986). Male rats had a NOAEL of 300 mg/m³ (75 ppm) and female rats a LOAEL of 100 mg/m³ (25 ppm). The IRIS RfC was obtained by calculating a BMCL₁₀, the 95% lower confidence limit on the extrapolated concentration where a minimal response (10%) occurs, adjusting the BMCL₁₀ for continuous exposure and applying the same interspecies and intraspecies uncertainty factors of 3 and 10. The BMCL₁₀ obtained was 39 mg/m³, adjusting for continuous exposure this is 6.9 mg/m³. Dividing this by the uncertainty factor of 30 gives the IRIS RfC of 0.2 mg/m³ (200 µg/m³).

In both scenarios exposure is to vapor phase VDC and the critical effect is to the liver, a systemic as opposed to site of entry effect. The inhalation guidance levels explicitly set the animal exposure concentration equal to a human equivalent exposure concentration following standard practice for a gas with systemic effects that is relatively insoluble and unreactive in the extrathoracic and tracheobronchial liquid and tissue (CalEPA 2000, USEPA 1994, USEPA 2002). This equality is a consequence of the default assumption that the ratio of the concentration in air to the concentration in the animal's blood is the same as that ratio in humans. In the USEPA toxicological review for VDC (USEPA 2001) it is noted that:

“The blood:air partition coefficient in rats is 5 (D’Souza and Andersen, 1988). No data are available to determine the blood:air partition coefficient in humans. Therefore, the default value of 1 is used for $(H_{b/g})_A/(H_{b/g})_H$.” and

“Using allometric scaling, D’Souza and Andersen (1988) calculated that the amount of 1,1-DCE epoxide formed in the human was fivefold lower than in the rat. This information, however, is not considered sufficient to reduce the interspecies UF to a value less than that provided by the use of inhalation dosimetry.”

The blood:air partition coefficient for a child's blood is likely to be nearly the same as the blood:air partition coefficient for adult blood. This suggests that, absent metabolic differences that change a child's sensitivity, a RfC derived for an adult chronic inhalation exposure to VDC would be adequate for assessing the significance of children's exposure.

Model for the amount of VDC in indoor air:

The source term is a first-order decay term; the loss term is due to bulk air exchange. The mass balance for well-mixed air gives:

$$(1) \quad \frac{dn_{air}}{dt} = k_1 n_{carpet} - n_{air} k_2$$

$$\frac{dn_{air}}{dt} = k_1 n_{c0} e^{-k_1 t} - n_{air} k_2$$

where k_1 is the first order rate constant for release from the carpet (hr^{-1}), k_2 is the air exchange rate (hr^{-1}), n_{carpet} is the amount of VDC in the carpet ($\mu\text{g}/\text{m}^2$) at time t (hr), n_{c0} is amount of VDC initially in the carpet ($\mu\text{g}/\text{m}^2$), and n_{air} is the amount of VDC in air ($\mu\text{g}/\text{m}^2$). Solving (1) subject to the initial condition $n_{\text{air}} = 0$ at $t = 0$ gives the amount in air as a function of time (Clausen 1993).

$$(2) \quad n_{\text{air}} = \frac{k_1 n_{c0}}{(k_2 - k_1)} [e^{-k_1 t} - e^{-k_2 t}]$$

Calculation of Exposure Concentration:

Scenario 1: Complete Release:

Assuming that the complete release is instantaneous, the release rate constant k_1 is very large, k_2 is negligible with respect to k_1 , $\exp(-k_1 t)$ is zero, and (2) reduces to

$$(3) \quad n_{\text{air}} = n_{c0} e^{-k_2 t}$$

The average amount in air during the time from $t = 0$ to t , n_{ave} , is given by integrating equation (3),

$$(4) \quad n_{\text{ave}} = \frac{n_{c0} (1 - e^{-k_2 t})}{k_2 t}$$

Converting units and substituting,

$$\begin{aligned} n_{c0} &= 3 \mu\text{g}/\text{g} \times 453.59 \text{ g}/\text{oz} \times 20 \text{ oz}/\text{yd}^2 / (0.83612 \text{ m}^2/\text{yd}^2) = 2034 \mu\text{g} \\ \text{VDC}/\text{m}^2 & \\ t &= 5 \text{ yr} \times 365.25 \text{ days}/\text{yr} \times 24 \text{ hr}/\text{day} = 43830 \text{ hr} \\ k_2 &= 0.3 \text{ hr}^{-1} \end{aligned}$$

gives,

$$n_{\text{ave}} = 0.1547 \mu\text{g}/\text{m}^2$$

For an eight-foot, 2.44 m, ceiling, the average air concentration is $0.0634 \mu\text{g}/\text{m}^3$.

Scenario 2: The rate of release from carpet is determined by a first-order rate constant, k_1 .

Integrating equation (2) gives the average amount in the air, n_{ave} :

$$(5) \quad n_{\text{ave}} = \frac{k_1 n_{c0}}{(k_2 - k_1) t} \left[\frac{1}{k_1} (1 - e^{-k_1 t}) - \frac{1}{k_2} (1 - e^{-k_2 t}) \right]$$

The release rate constant is assumed to correspond to a release half-life of 2 weeks, 1 year, or 5 years. The rate constant k_1 is equal to $\ln 2 / \text{half-life}$, and the release rate constants corresponding to half-lives of 2 weeks, 1 year, and 5 years, are 0.00206 , 7.9×10^{-5} , and $1.6 \times 10^{-5} \text{ hr}^{-1}$, respectively.

Substituting these and

$$\begin{aligned} n_{c0} &= 3 \mu\text{g}/\text{g} \times 453.59 \text{ g}/\text{oz} \times 20 \text{ oz}/\text{yd}^2 / (0.83612 \text{ m}^2/\text{yd}^2) = 2034 \mu\text{g} \\ \text{VDC}/\text{m}^2 & \\ t &= 5 \text{ yr} \times 365.25 \text{ days}/\text{yr} \times 24 \text{ hr}/\text{day} = 43830 \text{ hr} \\ k_2 &= 0.3 \text{ hr}^{-1} \end{aligned}$$

gives n_{ave} equal to 0.1545 , 0.149 , and $0.077 \mu\text{g}/\text{m}^2$, for the two-week, one-year, and five-year half-life, respectively.

For an eight-foot ceiling the average air concentrations are 0.0633, 0.061, 0.032 $\mu\text{g}/\text{m}^3$ for the two-week, one-year, and five-year half-lives.

Discussion:

In the first scenario all the VDC is released during the five-year replacement cycle of the carpet. The average air concentration for the five years was 0.0634 $\mu\text{g}/\text{m}^3$. This average does not depend on the timing of the release during the five years. If all the VDC were to be released within the first year, a higher average exposure concentration would not be obtained unless the carpets were replaced more frequently than every five years. Since average replacement times over a 70-year lifetime are very unlikely to be shorter than five years, higher average exposure concentrations are equally unlikely. Assuming that all the VDC is released at some point during the five-year carpet lifetime is a very conservative assumption.

The second scenario uses the more realistic assumption that the amount released from carpet declines in proportion to the amount remaining in the carpet. This gives an exponential decrease in the amount released as a function of time. For a half-life of less than a year, the 5-year averaging time represents five or more half-lives and essentially all the VDC in the carpet is released. For a longer half-life, less than all the VDC is released and the average air concentration is reduced. The average concentrations are 0.0633, 0.061, and 0.032 $\mu\text{g}/\text{m}^3$, for the two-week, one-year, and five-year half-lives for release from carpet.

Children have a greater inhalation rate per unit of body weight than adults. This can be a factor of as much as 3 or 4 for younger children. This greater relative inhalation rate only applies during childhood, a limited fraction of a lifetime. Weighted over a lifetime the greater relative inhalation is no more than 20 or 30%. Whether this implies a greater sensitivity for children depends on whether it implies a greater dose at the critical target. It is not clear that this is the case for a relatively insoluble, unreactive gas with systemic effects. Since guidance levels are expected to be accurate within an order of magnitude, the range of uncertainty around the guidance level includes the potential extra sensitivity of children due to greater relative inhalation.

The predicted average air concentration ranges from 0.032 $\mu\text{g}/\text{m}^3$ to 0.0634 $\mu\text{g}/\text{m}^3$. These are a factor of 1000 to 2000 less than the state of California chronic inhalation reference exposure level of 70 $\mu\text{g}/\text{m}^3$. The 5-year average concentrations obtained for release half-lives up to a year are essentially identical and slower release rates result in lower exposure concentrations of 0.0633, 0.061, 0.032 $\mu\text{g}/\text{m}^3$, for the 2-week, one-year, and five-year half-lives.

Mechanisms that change the concentration of a chemical in a room are likely. For example, an interior surface (walls) capable of VDC sorption and desorption would affect the air concentration. Assuming the VDC concentration on the walls is zero initially, the wall initially acts as a sink and this reduces the air concentration compared to the scenarios described above. Allowing sorption and desorption from interior surfaces can shift the VDC released from one carpet to the wall for release to air after the installation of another carpet. If exposure is averaged over several carpets the amount of VDC left in the wall at the end of the exposure period reduces the average air concentration relative to the first scenario where there is complete release and no sorption to walls. Mass balance considerations dictate that the highest average concentration is obtained when all the VDC is released over the life of each carpet, scenario one above.

Summary:

These calculations provide health protective conservative estimates of exposure to VDC monomer through the use of a VDC-containing polymer in carpet. Exposure concentration is conservatively estimated to range from 0.032 $\mu\text{g}/\text{m}^3$ to 0.064 $\mu\text{g}/\text{m}^3$, at least three orders of magnitude less than health protective chronic inhalation benchmarks. Since these are very much greater than the excess relative inhalation of children, these calculations demonstrate adequate health protective margins for the critical effect in children as well as adults. The calculations are not estimates of the actual levels of exposure because the evaluation relies on health protective overestimates of exposure concentrations. (Fontaine, D. D., 2002)

References:

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5.5 Estimated Aggregate Exposure

Since each of the scenarios above was constructed to give an overly conservative estimate of exposure, combining the exposures from these scenarios is a conservative method of estimating aggregate exposure. The important assumptions in the exposure scenarios above that lead to overestimating the exposure are summarized below.

The ambient air inhalation scenario used the measurable ambient air samples as a surrogate for inhaled air even though 90% of the 21,534 air samples did not contain measurable VDC. Using some fraction of an estimated detection limit for samples that were not quantified would greatly reduce the estimated exposure.

The indoor air inhalation scenario assumes that all floors are carpeted every five years with carpets that contain latex with the maximum manufacturing specification for content of VDC. No allowance is made for the loss of VDC during manufacture or distribution. It is assumed that all VDC is released into the interior living space and that this space has less than a typical residential air exchange rate. Carpet has a larger mass than most items in the home and therefore provides an overly conservative estimate of the amount of VDC available for release to indoor air.

The drinking water scenario assumes that all water contains at least the detection limit of VDC even though 98.5% of the 64,000 samples contain less than the detection limit. These concentrations are used as a surrogate for consumed water with no accounting for VDC that would be lost during distribution prior to reaching the tap.

Exposure to VDC via food was estimated assuming that all plastic wrap contained more than the typical manufacturing specification maximum VDC and all wrapped food extracted the VDC with same efficiency as one hour of exposure to 212° F peanut oil.

The aggregate exposure is obtained by combining the exposures from the scenarios for all relevant routes. To combine exposures from different routes they are put on a common basis. Since VDC is relatively well absorbed following inhalation, and since VDC at chronic exposure concentrations does not have a portal of entry critical effect, inhaled concentration was converted to dose assuming 100% absorption and the daily inhalation volumes normalized to body weight appropriate to the age group under consideration (CalEPA 2000). This gives both inhalation and oral doses in units of mass of VDC/body weight/day allowing aggregation over these routes by addition of the doses. However this method of combining the exposures by directly adding the results from the different routes is especially conservative when applied to the unlikely higher exposure results. The probability that several unlikely extreme exposures happen to the same individual is much lower than the probability that the individual experiences a single unlikely extreme exposure.

The aggregation of exposure chosen here gives a conservative estimate useful for a screening estimate of risk but does not provide an estimate of actual exposure. Since a distribution or range of exposure values is calculated for these scenarios both a central tendency and high end estimate are given for each exposure scenario. The central tendency estimates are obtained using mean or median values and may be interpreted as typical exposure estimates for the scenarios. The high end exposure estimates were obtained by selecting the 90th, 95th-tile, or extreme values from the results for the different scenarios. As noted above, this method of aggregating the exposures gives an overly conservative estimate of the exposure but not a quantitative estimate of the probability of the resultant aggregate exposure.

Estimated Aggregate Exposure for Children

	Central Tendency Exposure μg/kg/day	High End Exposure μg/kg/day
Ambient Air (20% of time) ⁱ	0.12 ^a 0.024	0.36 ^e 0.072
Indoor Air – Carpet (80% of time) ⁱ	0.028 ^b 0.023	0.034 ^f 0.027
Drinking Water	0.008 ^c	0.014 ^g
Oral – Food Wrap	0.010 ^d	0.0375 ^h
Total	0.065	0.15

^a The median value overestimate for children aged 1 to 18 years (Fontaine 2002a).

^b Obtained using the maximum air concentration of 0.063 μg/m³ (Fontaine 2002b) and the mean inhalation rate of children aged 1 to 12 years of 0.441 m³/kg/day (CalEPA 2000).

^c The median value overestimate for children aged 1 to 12 years (Fontaine 2002c).

^d Estimated using 1 kg of food only ingestion per day and a 20 kg child.

^e The 95th %-tile value for children aged 1 to 18 years (Fontaine 2002a).

^f Obtained using the overestimated air concentration of 0.063 μg/m³ (Fontaine 2002b) and the 90th %-tile inhalation rate of children aged 1 to 12 years of 0.5405 m³/kg/day (CalEPA 2000).

^g The 95th %-tile value for children aged 1 to 12 years (Fontaine 2002c).

^h Estimated using 3 kg of food and drink ingestion per day and a 20 kg child (Fontaine 2002d).

ⁱ Jenkins, Overview: California Indoor Exposures and Risk. Abstract Presented at Indoor Air Quality: Risk Reduction in the 21st Century.

References:

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Fontaine, D. D. (2002d) Potential Oral Exposure to Vinylidene Chloride from the Use of Food Wrap. Unpublished Research Note of The Dow Chemical Company.

5.6 Aggregate Exposure Summary

The aggregate exposure of children is obtained by the addition of the exposures from scenarios for all relevant routes. The exposure estimates from the air and water scenarios are based on large amounts of independently measured concentration data and this provides assurance that unknown sources are unlikely to have been overlooked. The addition of the exposures from the individual scenarios gives an overly conservative estimate of the aggregate exposure and also the probability of a high exposure. Even with the compounded conservatism of the method, the estimated exposures are extremely low. The typical childhood exposure for these conservative scenarios is 0.065 μg/kg/day. Even the direct addition of the low probability exposure

tails gives low exposure. The high end childhood exposure for these conservative scenarios is 0.15 µg/kg/day. Exposure to measurable quantities of VDC is shown to be infrequent, episodic, and at very low levels.

6.0 Hazard Assessment

6.1 Introduction

The potential toxicity of VDC has been extensively studied in a variety of assays and in a number of different species of test animals. Data has been generated on categories listed in all three Tiers of the VCCEP. The age and sources of many of these studies have ensured a heterogeneous database containing studies of varying sophistication and range. In many cases, multiple studies are available that individually or collectively provide a complete assessment of a particular VCCEP category for VDC. Conversely, numerous studies have provided data that is applicable to more than one VCCEP category, for example the evaluation of gonads and nervous and immune system tissues in repeated-dose toxicity studies provide assessments of potential reproductive toxicity, neurotoxicity and immunotoxicity, respectively. Most studies predate the advent of Good Laboratory Practices, however, many have been quite comprehensive in nature, even by today's guideline standards.

An overview of the test requirements for the categories making up the three tiers of VCCEP and the data available for VDC are provided in Text Table 6.1.1. Individual studies conducted on VDC have been outlined in the attached Robust Study Summaries and are reviewed below by general VCCEP categories. Thorough evaluations of potential acute oral and inhalation toxicity, repeated-dose toxicity (subchronic), mutagenicity, clastogenicity, developmental toxicity, reproductive toxicity, chronic toxicity/oncogenicity, and metabolism of VDC have been conducted and reported in peer-reviewed journals. The toxicity of VDC is primarily dependent upon a balance between its activation and detoxification via saturable enzymatic pathways that can be influenced by the nutritional state, body size and sex.

Text Table 6.1.1. Testing Requirements for Tiers 1-3 of VCCEP and Data Available on VDC.

TIER	TEST	VDC DATA AVAILABLE/RESULTS
1	Acute Oral or Acute Inhalation Toxicity.	Oral LD50 data in two species and 4-hour LC50 data in three species. Generally moderate acute toxicity; however, significant effects of fasting and sex reported.
1	<i>In Vitro</i> Gene Mutation (bacterial reverse mutation assay).	Numerous Guideline-quality <i>In Vitro</i> gene mutation assays, including mammalian cell mutagenesis studies. Generally demonstrating mutagenic activity in the presence of activating enzymes.
1&2	Reproductive Toxicity: <u>Tier 1</u> - Combined repeated dose toxicity with reproductive and	Guideline-quality rat multi-generation reproduction study.

	developmental screen or repeated-dose oral toxicity and one-generation reproductive toxicity. <u>Tier 2</u> – Reproduction and fertility effects. <u>Tier 2</u> – Prenatal developmental toxicity (two species).	Demonstrated lack of primary effect upon reproduction. Also, multiple subacute, subchronic and chronic toxicity studies in rats, mice, hamsters, rabbits, dogs and/or monkeys conducted. Demonstrated a lack of treatment-related effects upon gonads and secondary sex organs.
1	<i>In Vitro</i> or <i>In Vivo</i> Chromosomal Aberrations or <i>In Vivo</i> Micronucleus.	Numerous cytogenetics studies in cultured mammalian cells. Generally resulted in positive findings and <i>in vivo</i> cytogenetic and micronucleus studies demonstrating a lack of activity.
2	Repeated Dose (Subchronic) Toxicity.	Multiple Guideline-quality subacute, subchronic and chronic toxicity studies in rats, mice, hamsters, rabbits, dogs and/or monkeys, under a variety of dosing routes and regimens. Liver and kidney identified as primary target tissues.
2	Developmental Toxicity (two species)	Guideline-quality studies of developmental toxicity in rats and rabbits. Demonstrated fetotoxicity at or above maternally toxic exposure levels and a lack of developmental toxicity.
2	<i>In Vivo</i> Mammalian Bone Marrow or Erythrocyte Micronucleus (if <i>in vitro</i> Tier 1 tests positive) Cytogenetic Toxicity.	Multiple studies examining potential chromosomal toxicity under a variety of dosing routes, regimens and target cells. Generally demonstrating a lack of cytogenetic toxicity.
2	Immunotoxicity	No specific guideline study; however, gross and histopathological examination of immune system tissues as part of multiple subacute, subchronic and chronic toxicity studies. Revealed no treatment-related effects. Reported immunosuppressive activity of sera of VDC-treated mice shown to be

		<u>secondary</u> to significant tissue damage and mediated by related elevations in serum immunosuppressive cytokines.
2	Metabolism and Pharmacokinetics	<p>Guideline-quality studies of absorption, metabolism, distribution and excretion in rats, including metabolite identification, following oral or inhalation administration.</p> <p>Demonstrated the rapid absorption, metabolism and excretion of VDC. Interspecies comparisons of metabolism and relationship to potential toxicity also demonstrated. Pharmacokinetics well defined and PBPK model(s) generated.</p>
3	Carcinogenicity or Combined Chronic Toxicity/Carcinogenicity	<p>Multiple studies, several Guideline-quality, have been conducted in rats, mice and/or hamsters under a variety of dosing routes and regimens, including <i>in utero</i> exposure.</p> <p>Demonstrated a lack of carcinogenic potential. Reports of increased incidences of kidney tumors in some studies not reproduced in more comprehensive, Guideline-quality studies.</p>
3	Neurotoxicity Screening Battery	<p>No specific guideline study; however, multiple guideline-quality subacute, subchronic and chronic toxicity studies undertaken that have included examination of central and peripheral nervous tissues.</p> <p>No indication of the nervous systems as primary target tissues.</p>
3	Developmental Neurotoxicity	<p>No specific guideline study; however, a developmental toxicity study specifically examining potential effects of <i>in utero</i> exposure to VDC upon behavioral endpoints has been reported.</p> <p>No effects were observed.</p> <p>In addition, soft tissue examination of fetuses in guideline-quality developmental toxicity studies.</p>

	No indication of a primary effect upon the nervous system during development.
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6.2 Acute Toxicity (Tier 1)

The potential acute toxicity of VDC as defined by lethality has been well characterized via the oral and inhalation routes of exposure. No further evaluation of the potential acute oral or inhalation toxicity of VDC is warranted at this time.

Oral.

Several independent studies evaluating the acute oral toxicity of VDC have been conducted in both sexes of rats and mice. Studies were generally conducted prior to GLP requirements using a number of protocols and strains of rats. Extensive experimental detail consistent with a guideline study was not available for these studies; however, findings were published in peer-reviewed journals and the remarkably consistent results between studies suggest that a high degree of confidence may be placed in them. As shown in Text Table 6.2.1, calculated oral LD50 values in rats ranged from 800 to 2000 mg/kg for both sexes with an overall average of approximately 1500 mg/kg. Consistent with known differences in extent of VDC metabolism, the acute oral toxicity of VDC was considerably greater for mice (lower LD50 values) than for rats. There was no indication of a significant sex-related difference in mortality in either species. In contrast, Anderson and Jenkins (1977) have demonstrated a significant body weight and sex effect upon acute toxicity and lethality of orally administered VDC. Smaller, leaner male Holtzman HOT: (SD)BR rats were found to be much more susceptible to hepatotoxic effects of VDC than larger, heavier animals, but only within a specific range of dosages. Females were considerably more resistant to the toxic effects of VDC than males. It was concluded that acute toxicity reflected a balance between metabolic activation and detoxification of VDC and its metabolites.

Text Table 6.2.1. Acute Oral Toxicity Studies on VDC Conducted in Rats and Mice.

Study	Species	Calculated LD50	Reference
Oral Gavage (sex not noted; corn oil vehicle)	Rat (male)	1510 mg/kg	(Jenkins <i>et al.</i> , 1972)
Oral Gavage	Rat (male)	800-2000 mg/kg	(Andersen and Jenkins, 1977)
Oral Gavage	Rat (male)	1550 mg/kg	(Jenkins <i>et al.</i> , 1972)
Oral Gavage	Rat (male, female)	1800 mg/kg (M) 1500 mg/kg (F)	(Ponomarev and Tomatis, 1980)
Oral Gavage	Mouse (male, female)	201-235 mg/kg (M) 171-221 mg/kg (F)	(BUA Stoffbericht 33, 1988; Jones and Hathway, 1978)

Inhalation.

Several independent studies evaluating the acute toxicity of inhaled VDC vapor have been conducted in both sexes of rats, mice and hamsters. Studies were conducted prior to GLP requirements thus extensive experimental detail consistent with a guideline study is not available for most studies. Despite this, most findings have been published in peer-reviewed journals. As shown in Text Table 6.2.2, a relatively wide range of calculated 4-hour LC50 values for VDC have been reported with most in excess of several thousand ppm (>500 mg/m³). Species, sex and nutritional status effects upon acute inhalation toxicity have been noted, consistent with known effects of these factors

upon the metabolism of VDC. In general in comparable studies, inhaled VDC vapor was more toxic to mice and least to rats with hamsters displaying intermediate sensitivity. LC50 values in both fasted and nonfasted mice ranged from 140 to 820 mg/m³ (35-207 ppm), hamsters from 600-11700 mg/m³ (151-2947 ppm), and rats from 1600 to 128000 mg/m³ (403-32242 ppm). The theoretical saturated atmosphere for VDC at 25°C is approximately 3050000 mg/m³ (770,000 ppm). Males were generally 1.5-3 fold more sensitive than females across all species independent of nutritional status with the exception of fasted male rats in which a significant interaction of sex and nutritional status were evident. LC50 values for fasted male rats were over 10-fold less than those of fasted females. In comparable studies, fasting was reported to lower the LC50 by 2-3 fold in both sexes of mice, 6-10 fold in both sexes of hamsters, 2-3 fold in female rats and 18-25 fold in male rats. Fasting has been demonstrated to decrease the potential of an animal to detoxify VDC and its metabolites by decreasing levels of glutathione thereby increasing the toxicity of VDC (Anderson and Jenkins, 1977 and references therein; metabolism section).

Text Table 6.2.2. Acute Inhalation Toxicity Studies on VDC Conducted in Rats, Mice and Hamsters.

Study	Species	Calculated LC50	Reference
4-Hour Vapor	Rat (Sprague-Dawley males)	1600 mg/m ³ (403 ppm)	(Leach, 1963; Miller and Tainter, 1944; Siegel <i>et al.</i> , 1977)
4-Hour Vapor	Rat (fasted male, fasted female)	1600 mg/m ³ (403 ppm) (M) 26000 mg/m ³ (6549 ppm) (F)	(BASF AG, 1979)
4-Hour Vapor	Rat (nonfasted male, nonfasted female)	28400 mg/m ³ (7254 ppm) (M) 40800 mg/m ³ (10277 ppm) (F)	(BASF AG, 1979)
Vapor (duration not indicated)	Rat (nonfasted male, nonfasted female)	128000 mg/m ³ (32242 ppm) (M&F)	(Carpenter <i>et al.</i> , 1949; Siegel <i>et al.</i> , 1971)
Vapor (duration presumed 4 hours)	Rat (nonfasted and fasted males)	60000 mg/m ³ (15113 ppm) (nonfasted M) 2400 mg/m ³ (605 ppm) (fasted M)	(Jaeger <i>et al.</i> , 1974)
Vapor (duration presumed 4 hours)	Rat (nonfasted male)	60000 mg/m ³ (15113 ppm) (M)	(Jaeger <i>et al.</i> , 1973)
3-Min Vapor	Rat (sex not identified)	Mortality of 8/12 rats in saturated atmosphere.	(BASF AG, 1979)
22-Hour Vapor	Mouse (CD-1 males)	400 mg/m ³ (98 ppm)	(Short <i>et al.</i> , 1977)
4-Hour Vapor	Mouse (fasted male, fasted female)	200 mg/m ³ (50 ppm) (M) 500 mg/m ³ (126 ppm) (F)	(BASF AG, 1979)
4-Hour Vapor	Mouse (nonfasted male, nonfasted female)	460 mg/m ³ (116 ppm) (M) 820 mg/m ³ (207 ppm) (F)	(BASF, 1979)
4-Hour Vapor	Mouse (fasted	140 mg/m ³ (35 ppm) (M)	(Short <i>et al.</i> , 1977)

	male, fasted female)	420 mg/m ³ (106 ppm) (F)	
4-Hour Vapor	Hamster (nonfasted male, nonfasted female)	6600 mg/m ³ (1663 ppm) (M) 11700 mg/m ³ (2947 ppm) (F)	(BASF AG, 1978)
4-Hour Vapor	Hamster (fasted male, fasted female)	600 mg/m ³ (151 ppm) (M) 1800 mg/m ³ (453 ppm) (F)	(Anderson <i>et al.</i> , 1979)

6.3 Gene Mutation (Tier 1)

The potential genotoxicity of VDC as defined by mutagenic activity has been extensively evaluated in numerous *in vitro* and *in vivo* assays (see Text Table 6.3.1). A number of studies have been reported in great detail, albeit previous to promulgation of GLP guidelines, and the results of many have been published in peer-reviewed journals. Assays have ranged from classic *in vitro* bacterial mutagenicity tests employing a variety of bacterial tester strains and several mammalian cell tests to hybrid tests in which tester strains of bacteria are exposed to VDC and metabolites in mice administered high dosages of VDC. Nearly all *in vitro* assays have yielded positive findings, especially when mammalian enzymes capable of metabolizing VDC were included in the incubation mixtures. In instances where the added enzymes were from animals administered compounds known to induce the activation of VDC, mutagenic activity was increased relative to assays employing untreated mouse enzymes. In other instances pretreatment of mice with compounds known to induce Phase II enzymes decreased the mutagenic activity of VDC. Human liver enzymes were demonstrated to be capable of activating VDC to a mutagenic metabolite(s) under the conditions of the assays employed. In contrast, *in vivo* mutagenicity assays conducted in rats, mice and *Drosophila* (sex-linked lethal mutation assays) have been negative. No further evaluation of VDC mutagenic potential is warranted at this time.

Text Table 6.3.1. Mutagenicity Assays of VDC.

Study	Test	Results	Reference
Bacterial Mutagenicity	Ames' Assay in <i>Salmonella typhimurium</i> tester strains TA1535, 1537, 98, 100 and 92 using 375-22500 ppm VDC vapor (added liver S-9 from several strains of mice, hamster, rat, human)	Positive. Response with mouse> hamster> rat> human activation. Added GSH decreased response 50%.	(BASF AG, 1983; Oesch <i>et al.</i> , 1983)
Bacterial Mutagenicity	Ames' Assay in <i>Salmonella typhimurium</i> tester strains TA1535, 100 using 0.2-20% VDC vapor (added liver S-9 from OF-1 mice)	Positive. Exclusion of NADPH eliminated activity.	(Bartsch <i>et al.</i> , 1975; World Health Organization, 1990)
Bacterial Mutagenicity	Ames' Assay in <i>Salmonella typhimurium</i> tester	Positive. Pretreatment of rats with known inducers	(Bartsch <i>et al.</i> , 1979; World Health Organization, 1990)

	strains TA1530, 100 using 2 and/or 20% VDC vapor (added liver S-9 from several species)	of Phase I and II enzymes increased and decreased activity, respectively.	
Bacterial Mutagenicity	Ames' Assay in <i>Salmonella typhimurium</i> tester strains TA1530 using 5% VDC vapor (added liver S-9 from several species)	Positive in mice and humans on long-term PB therapy, negative in monkeys and humans.	(Jones and Hathway, 1978; Le Blanc, 1980)
Bacterial Mutagenicity	Several Ames' Assays in one or more <i>Salmonella typhimurium</i> tester strains using VDC vapor or direct addition to incubation mix in DMSO (with or without added liver S-9 from various species)	Positive with or without added S-9.	(Malaveille <i>et al.</i> , 1977; Waskele, 1978; McCarroll <i>et al.</i> , 1983; Cerna and Kypenova, 1977; Baden, 1976; Baden, 1982; Baden, 1978; World Health Organization, 1990)
Bacterial Mutagenicity	<i>Escherichia coli</i> WP2 uvrA Assay using 375-22500 ppm VDC vapor (added liver S-9 from various species).	Positive.	(BASF AG, 1983; Oesch <i>et al.</i> , 1983)
Bacterial Mutagenicity	<i>Escherichia coli</i> K12 Assay using 2.5 mM VDC vapor (addition of S-9 not reported).	Positive.	(Greim <i>et al.</i> , 1975; World Health Organization, 1990)
Bacterial Mutagenicity	<i>Escherichia coli</i> WP2 uvrA, pKM 101 Assay using 2000 or 4000 mg/m ³ VDC vapor (with or without S-9).	Positive with S-9.	(Greim <i>et al.</i> , 1975; World Health Organization, 1990)
Yeast Mutagenicity	<i>Saacharomyces cerevisiae</i> D7 and D61.M Assay (with or without mouse liver S-9)	Positive in D7 with S-9.	(Koch <i>et al.</i> , 1988)
Yeast Mutagenicity	<i>Saacharomyces cerevisiae</i> D7 Assay using 0-50 mM VDC solution (with or without PCB-induced mouse liver	Positive with S-9.	(Bronzetti <i>et al.</i> , 1981; World Health Organization, 1990)

	S-9)		
Host-Mediated Bacterial Mutagenicity	Mice dosed with LD50 or half-LD50 VDC and <i>S. typhimurium</i> TA1590,1591,1592.	Positive.	(Cerna and Kypenova, 1977)
Host Mediated Yeast Mutagenicity	Mice, dosed with single high or multiple lower doses VDC and "yeast cells"	Positive.	(Bronzetti <i>et al.</i> , 1981; World Health Organization, 1990)
Mammalian Cell Mutagenicity	Mouse Lymphoma Assay using 40-603 mg/L in solution (with or without S-9)	Positive (with S-9 > without S-9).	(McGregor <i>et al.</i> , 1991)
Mammalian Cell Mutagenicity	Chinese Hamster V79 (with or without S-9 from rats or mice dosed with PB)	Negative.	(Drevon and Kuroki, 1979; World Health Organization, 1990)
Dominant Lethal Mutation Assay	Male rats exposed to 220 mg/m ³ VDC vapor, 6 hr/day, 5 days/wk, 11 weeks with subsequent matings.	Negative.	(Short <i>et al.</i> , 1977; World Health Organization, 1990)
Dominant Lethal Mutation Assay	Male mice exposed to 40-200 mg/m ³ VDC vapor, 6 hr/day, 5 days with subsequent mating.	Negative.	(Anderson <i>et al.</i> , 1977; World Health Organization, 1990)
Sex-Linked Recessive Lethal Mutation Assay	<i>Drosophila melanogaster</i> males given feed containing 25000 ppm VDC or injected with VDC (dose not provided).	Negative.	(Foureman <i>et al.</i> , 1994)

6. 4 Cytogenetics (Tiers 1 and 2)

The potential genotoxicity of VDC as defined by clastogenic activity has been extensively evaluated in numerous *in vitro* and *in vivo* assays (see Text Table 6.4.1). A majority of these studies, while not following GLP guidelines, have followed established testing procedures and been reported in peer-reviewed journals. Assays have ranged from the exposure of cultured mammalian-derived cell lines to VDC solutions or vapor *in vitro*, to whole animal assays. The former were reported to be nearly uniformly positive, in the presence of metabolic activation systems, while the latter have been uniformly negative. No further *in vitro* or *in vivo* evaluation of VDC cytogenetic toxicity potential is warranted at this time.

Text Table 6.4.1. *In Vitro* and *In Vivo* Cytogenetics Assays of VDC.

Study	Test	Results	Reference
<i>In Vitro</i> Mammalian Cell Cytogenetics	CHL Chromosome Aberration Assay using 0-1.5 mg/mL VDC solution (with or without S-9).	Positive with metabolic activation.	(Sawanda <i>et al.</i> , 1987)
<i>In Vitro</i> Mammalian Cell Cytogenetics	CHL Cell Sister Chromatid Exchange Assay using 0-1.0 mg/mL (without S-9) and 0-0.1 mg/mL (without S-9)	Positive with metabolic activation.	(Sawanda <i>et al.</i> , 1987)
<i>In Vitro</i> Mammalian Cell Cytogenetics	CHO Cell Sister Chromatid Exchange Assay using 1.8-7.0% VDC vapor (with S-9)	Positive with metabolic activation.	(McCarroll <i>et al.</i> , 1983; World Health Organization, 1990)
<i>In Vitro</i> Mammalian Cell Cytogenetics	CHL Cell Sister Chromatid Exchange Assay using 0-2 mg/mL (with and without PCB-induced rat liver S-9).	Positive with metabolic activation.	(Sawanda <i>et al.</i> , 1987; World Health Organization, 1990)
<i>In Vivo</i> Mammalian Cytogenetics	Male Mouse Bone Marrow Micronucleus Assay at 0-200 mg/kg acute or 0-100 mg/kg/day for 4 days.	Negative.	(Sawanda <i>et al.</i> , 1987; World Health Organization, 1990)
<i>In Vivo</i> Mammalian Cytogenetics	Chromosome aberration assay in male and female rats inhaling 0.1 or 300 mg/m ³ VDC vapor for 6 months.	Negative.	(Quast <i>et al.</i> , 1986; World Health Organization, 1990)
<i>In Vivo</i> Mammalian Cytogenetics	Chromosome aberration assay in female mice injected ip acutely with half LD50 or 5 times with a sixth LD50 VDC.	Negative.	(Cerna and Kypenova, 1977; World Health Organization, 1990)
<i>In Vivo</i> Mammalian Cytogenetics	Chromosome aberration assay in mice and rats inhaling 220 mg/m ³ VDC vapor 6 hr/day, 5 days/wk, 12 months.	Negative.	(Lee <i>et al.</i> , 1977; World Health Organization, 1990)
<i>In Vivo</i> Mammalian Cytogenetics	Chromosome aberration assay in	Negative.	(BASF AG, 1975)

	bone marrow of male and female hamsters dosed acutely po with 178 uL/kg VDC.		
<i>In Vivo</i> Mammalian Cytogenetics	Chromosome aberration assay in bone marrow of male and female hamsters inhaling 120-400 mg/ m ³ VDC vapor, 6 hr.day, 5 days/wk, 29 exposures.	Negative.	(BASF AG, 1976)

6.5 Repeated-Dose Toxicity (Tiers 1 and 2)

Numerous independent studies evaluating the repeated dose toxicity of inhaled or orally administered VDC have been conducted in both sexes of rats, mice, hamsters, rabbits, dogs and monkeys. Studies were conducted prior to GLP requirements and extensive experimental designs consistent with guideline studies are not available for most studies. Despite this, most findings have been published in peer-reviewed journals. As shown in Text Table 6.5.1, a relatively wide range of dosing or exposure regimens and dosing periods have been employed. In general, the liver and kidneys appear to be the target tissues most often identified following repeated oral or inhalation exposure to VDC. A particularly comprehensive evaluation of chronic toxicity was conducted by Quast *et al.* (1986) (122) and Rampy *et al.* (1977, 1978) (123,124).

Text Table 6.5.1. Subacute, Subchronic and Chronic Repeated-Dose Toxicity Studies on VDC.

<u>Study</u>	<u>Design</u>	<u>NOEL or NOAEL [target tissue(s)]</u>	<u>Reference</u>
Inhalation	Rats (male and female Long Evans and Sprague-Dawley) exposed to 400 mg/m ³ (101 ppm) 8 hours/day for 6 weeks; 20-190 mg/ m ³ (5-48 ppm) continuous for 13 weeks.	400 mg/m ³ Continuous [possible pulmonary congestion]; presumptive 100 mg/ m ³ noncontinuous [liver and kidney histopathology].	(ECETOC, 1985; Prendergast <i>et al.</i> , 1967; World Health Organization, 1990)
Inhalation	Rats (M&F Sprague-Dawley) exposed to 120 (30 ppm) or 400 mg/m ³ (101 ppm) 6 hours/day, 5 days/week, for 6 weeks.	120 mg/m ³ [liver and kidney Wts., kidney histopathology].	(BASF AG, 1979)
Inhalation	Rats (M&F Sprague-Dawley) exposed to 100 (25 ppm) or 300 mg/m ³ (76 ppm) 6 hours/day, 5	<100 mg/m ³ [minor liver histopathology].	(Norris, 1977; Quast <i>et al.</i> , 1977; World Health Organization, 1990)

	days/week, for 90 days.		
Inhalation	Rats (M&F Alderley Park) exposed to 0.2 (50 ppm) or 800 mg/m ³ (202 ppm) 6 hours/day for 20 days.	<200 mg/m ³ [nasal mucosa and liver histopathology].	(ECETOC, 1985; Gage, 1970; World Health Organization, 1990)
Inhalation	Rats (M&F Sprague-Dawley) exposed to 40-100 mg/m ³ (10-25 ppm) or 160-300 mg/m ³ (40-75 ppm) 6 hours/day, 5 days/week, for 6, 12 or 18 months (the latter followed by a 6 month observation period).	<100 mg/m ³ [reversible liver histopathology].	(Quast <i>et al.</i> , 1986; Rampy <i>et al.</i> , 1977; Rampy <i>et al.</i> , 1978; World Health Organization, 1990)
Inhalation	Rats (M&F Sprague-Dawley) exposed to 40-800 mg/m ³ (10-202 ppm) 4 hours/day, 4-5 days/week, for 12 months .	400 mg/m ³ [liver histopathology].	(Maltoni <i>et al.</i> , 1984; World Health Organization, 1990)
Inhalation	Rats (M&F CD) exposed to 220 mg/m ³ (55 ppm) 6 hours/day, 5 days/week, for 12 months .	<220 mg/m ³ [liver histopathology].	(Lee <i>et al.</i> , 1977; World Health Organization, 1990)
Oral (drinking water)	Rats (M&F Sprague-Dawley) provided 60-200 mg/ L imbibed for 90 days.	60 mg/L [liver histopathology].	(Norris, 1977; Quast <i>et al.</i> , 1977; World Health Organization, 1990)
Oral (drinking water)	Rats (M&F Sprague-Dawley) provided 7-20 mg/kg/day (M) or 9-30 (F) imbibed for 24 months.	Males: 10 mg/L [liver histopathology] Females: <9 mg/kg/day [liver histopathology].	(Rampy <i>et al.</i> , 1977; Rampy <i>et al.</i> , 1978; Quast <i>et al.</i> , 1983; World Health Organization, 1990)
Oral (gavage)	Rats (M Wistar) administered 125 mg/kg/day (2 weeks), subsequently 200 mg/kg/day (2 weeks) 2 time/week.	<200 mg/kg/day [liver, mortality].	(Siegers <i>et al.</i> , 1983, World Health Organization, 1990)
Oral (gavage)	Rats (M&F F344/N) and Mice (M&F B6C3F1/N) administered 1 or 5	Rat: 1 mg/kg/day [kidney histopathology] Mice: <1 mg/kg/day	(National Toxicology Program, 1982; World Health Organization, 1990)

	mg/kg/day 5 days/week for 24 months.	[liver histopathology].	
Oral (gavage)	Rats (M&F F344/N) and Mice (M&F B6C3F1/N) administered 5-250 mg/kg/day 5 days/week for 13 weeks.	Rat: 5 mg/kg/day [liver histopathology] Mice: 15 mg/kg/day [liver histopathology].	(National Toxicology Program, 1982)
Oral (drinking water)	Rats (M&F Sprague-Dawley) administered 0.5-20 mg/kg/day 7 days/week for 28 days.	>20 mg/kg/day [none].	(Maltoni and Patella, 1983; World Health Organization, 1990)
<i>In Utero</i> and oral (gavage)	Rats (M&F BDIV) exposed <i>in utero</i> as dams administered acute oral dosage of 50 mg/kg on gd 17 and dosed 50 mg/kg/day for 120 days of age.	<50 mg/kg/day [liver and kidney].	(Ponomarkov and Tomatis, 1980; World Health Organization, 1990)
Inhalation	<u>Mice</u> (M&F Swiss, Balb/c, C3H) and <u>Rats</u> (M&F Sprague-Dawley) exposed to 40-800 mg/m ³ (10-202 ppm) 4 hours/day, 4-5 days/week, for up to 28 days. <u>Hamster</u> (Chinese) exposed to 100 mg/m ³ (25 ppm) 4 hours/day, 4-5 days/week, for 28 days.	<u>Mice</u> [liver and kidney, mortality]. <u>Hamster</u> [liver and kidney histopathology].	(Maltoni and Patella, 1983; World Health Organization, 1990)
Inhalation	Mice (M&F Swiss) exposed to 40-800 mg/m ³ (10-202 ppm) 4 hours/day, 4-5 days/week, for 12 months.	[liver histopathology].	(Maltoni <i>et al.</i> , 1984; World Health Organization, 1990)
Inhalation	Mice (M&F CD-1) exposed to 200 mg/m ³ (50 ppm) 6 hours/day, 5 days/week, for 6 months.	[mortality only].	(Hong, 1981; World Health Organization, 1990)
Inhalation	Mice (M&F CD-1) exposed to 220	[liver histopathology].	(Lee <i>et al.</i> , 1977; World Health

	mg/m ³ (55 ppm) 6 hours/day, 5 days/week, for 12 months.		Organization, 1990) (127,96)
Inhalation	Hamsters (M&F Chinese) exposed to 100 mg/m ³ (25 ppm) 4 hours/day, 4-5 days/week, for 12 months.	[none reported].	(Maltoni <i>et al.</i> , 1984; World Health Organization, 1990)
Inhalation	<u>Rabbit</u> (NZ White) exposed to 100 mg/m ³ (25 ppm) (continuous) or 400 mg/m ³ (101 ppm) 8 hours/day, 5 days/week, for 30 exposures. <u>Dogs</u> (beagle), <u>Guinea pig</u> (Hartley) and <u>Monkeys</u> exposed to 200 mg/m ³ (50 ppm) (continuous) or 400 mg/m ³ (101 ppm) 8 hours/day, 5 days/week, for 30 exposures.	<u>Rabbit</u> : Continuous: <0100 mg/m ³ [liver histopathology]. Repeated: 400 mg/m ³ [possibly pulmonary congestion] <u>Dogs</u> : Continuous: <200 mg/m ³ [liver histopathology]. Repeated: 400 mg/m ³ .	(ECETOC, 1985; Prendergast <i>et al.</i> , 1967; World Health Organization, 1990)
Inhalation	Rabbits exposed to 500-2000 mg/m ³ (126-504 ppm) 3 hours/day for 4 months.	[bronchitis, liver and kidney histopathology].	(Lazarev, 1960; World Health Organization, 1990)
Oral (capsule)	Dog (M&F beagle) administered 6.25-25 mg/kg/day daily for 97 days.	>25 mg/kg/day [none].	(DFG, 1985; Quast <i>et al.</i> , 1983; World Health Organization, 1990)
Inhalation	Mouse (M&F Ha(ICR), CD-1, CF-W, B6C3F1) exposed to 220-800 mg/m ³ (55-202 ppm) 6 hours/day, 5 days/week, for 2 weeks.	[Males: kidney histopathology, mortality] [Females: liver histopathology, mortality].	(Norris and Reitzk, 1984; World Health Organization, 1990)

6.6 Reproductive Toxicity (Tiers 1 and 2)

An extensive examination of the potential of VDC to inhibit reproductive success of animals in terms of toxicity to gonadal and secondary sex organs, and the ability to conceive, deliver and rear young have been examined. No direct toxic effects of VDC, either administered orally or via inhalation of vapor, upon reproductive organs or secondary sex tissues have been reported in rats, mice, guinea pigs, rabbits, dogs or

monkeys in the numerous subacute, subchronic and chronic repeated-dose studies (see appropriate sections).

A particularly significant and comprehensive reproduction study spanning 3-generations with a total of 7 matings and litters has been conducted in Sprague-Dawley rats imbibing VDC via their drinking water (50, 100 or 200 ppm) (Nitschke *et al.*, 1983). While the study was conducted prior to GLP and modern guidelines, a considerable amount of experimental detail is available, and the results were published in a peer-reviewed journal. Pups from all seven litters were exposed to VDC during conception, gestation, and nursing. Three generations of males and females were exposed for approximately 100 days pre-mating, in males ensuring exposure during a whole spermatogenic cycle. F0, F1b and F2 generations were mated to produce the F1a, F1b, F2, F3a, F3b and F3c litters. F1a, F3a and F3b litters were administered VDC until weaning and sacrifice on post-natal day 21-24. Male and female F3c rats were sacrificed at 185-213 days of age and continuous dosing. Gross and histopathological examinations of tissues, including gonads, were undertaken for every generation and litter. No consistent treatment-related effects upon body weights or feed or water consumption were observed. A possible decreased fertility was noted in F0 dams imbibing 200 ppm VDC water; however this was not found for dams producing the F2, F3a, F3b and F3c litters. No effects occurred on litter size, sex-ratio or pup growth. Likewise, no reproducible effect upon neonatal survival was noted in the study. No histopathological changes were observed in pups while only mild hepatotoxicity was noted in adult F1 and F2 rats. These findings are consistent with the known metabolic activation of VDC and the general lack of MFO activity in neonate animals. The NOELs/NOAELs for adults was determined to be 100 ppm for adult males and females and >200 ppm for neonates.

6.7 Developmental Toxicity (Tier 2)

Numerous studies evaluating the potential developmental toxicity of VDC employing different species, designs, routes have been reported (see Text Table 6.7.1). Gravid rats and rabbits and their developing fetuses have been administered up to maternally toxic levels of VDC vapors 7 hours/day via inhalation, gravid rats continuously via their drinking water, and gravid rats and mice to VDC vapor via inhalation under a continuous exposure regimen (23 hours/day).

Several instances of increased incidences of skeletal variations were reported in fetuses at maternally toxic dose/exposure levels (Murray *et al.*, 1979; Short *et al.*, 1977). These changes, including occurrences of wavy ribs and delayed ossification of sternbrae, reflect delayed development of fetal bone tissue typical of those observed in cases where maternal toxicity evidenced by decreased weight gain or loss or pathological changes have been noted in dams. Fetal skeletal variations are not generally considered to be indications of developmental toxicity. The one instance where an increase in a recognized teratogenic effect was noted in fetuses of VDC exposed animals was the occurrence of various forms of hydrocephalia by Short *et al.* (1977) (193) in Sprague-Dawley rats continuously exposed (23 hour/day) to VDC vapor. This change was seen coincident with significant maternal toxicity, including loss of body weight and mortality, and in which numbers of litters and fetuses were significantly decreased. It was concluded that VDC was "only a weak teratogen with little primary effect on development". Similar findings, even in the presence of delayed ossification, have not been reported in subsequent developmental toxicity studies of VDC.

Significantly, a portion of the Short *et al.* (1977) developmental study was specifically designed to examine potential behavioral effects upon rats exposed to VDC *in utero*.

The conclusion of the study was that “no problems with neural development, as measured by behavioral parameters, were observed”.

In contrast to findings in other developmental toxicity studies, Dawson *et al.* (1990; 1993) have reported an increase in total cardiac anomalies in rats exposed to VDC *in utero* via drinking water administered Sprague-Dawley dams or via direct infusion into the gravid uterus of rats by osmotic pump. An incidence of total cardiac malformations of 12-13% was recorded in pups from rats imbibing water containing either 0.15 ppm or 110 ppm VDC over a period of 2 months prior to and subsequently the whole pregnancy period (Dawson *et al.*, 1993). Controls had a 3% incidence of similar cardiac anomalies. An increased incidence of cardiac terata was also reported earlier by this group utilizing an extreme method of continuous infusion of VDC directly into the gravid rat uterus via implanted osmotic pumps (Dawson *et al.*, 1990). No other increases in malformations were found. However, a similar finding by this group with trichloroethylene have not been reproduced in a high-dose bolus dosing study at 500 mg/kg by Fisher *et al.* (2001) nor in a guideline inhalation developmental toxicity study in rats inhaling up to 3220 mg/m³ (600 ppm) by Carney *et al.* (2001). Further, the findings of Dawson *et al.* have been criticized by the IRIS Peer Review Workshop (2001) for lack of dose-response, high control rates of malformations, lack of specificity and a number of quality control problems. The draft EPA Integrated Risk Information System (EPA, 2000) concludes that “the changes reported by Dawson *et al.* (1993) must be assumed at this point to represent variations in cardiac morphology that have little or no physiological consequence”.

Text Table 6.7.1. Developmental Toxicity Studies on VDC.

<u>Study</u>	<u>Design</u>	<u>Maternal NOAEL & Developmental NOAEL</u>	<u>Reference</u>
Inhalation	Gravid rats (Sprague-Dawley) exposed to 80-640 mg/m ³ (20-160 ppm) 7 hours/day for gd 6-16.	Maternal: 80 mg/m ³ Fetal: 80 mg/m ³ Developmental: >640 mg/m ³ .	(Murray <i>et al.</i> , 1979; World Health Organization, 1990; TSCATS, 1992)
Inhalation	Gravid rats (CD ^a) exposed to 60-1800 mg/m ³ (15-453 ppm) continuous (22-23 hours/day) for gd 6-16.	Maternal: <60 mg/m ³ Fetal: <60 mg/m ³ Developmental: <60 mg/m ³ based upon delayed ossification and hydrocephalia ^b .	(Short <i>et al.</i> , 1977; World Health Organization, 1990)
Inhalation	Behavioral study of pups by exposing gravid rats (CD) to 200-1100 mg/m ³ (50-277 ppm) continuous (22-23 hours/day) for gd 8-20.	No behavioral effects observed.	(Short <i>et al.</i> , 1977; World Health Organization, 1990)
Inhalation	Gravid mice (CD-1) exposed to 60-1800 mg/m ³ (15-453 ppm) continuous (22-23	Maternal: 60 mg/m ³ Fetal: <60 mg/m ³ Developmental: <60 mg/m ³ based upon	(Short <i>et al.</i> , 1977; World Health Organization, 1990)

	hours/day) for gd 8-20.	delayed ossification ^b .	
Inhalation	Gravid rabbits (New Zealand White) exposed to 320 or 640 mg/m ³ (80 or 160 ppm) continuous (7 hours/day) for gd 6-18.	Maternal: 320 mg/m ³ Fetal: 320mg/ m ³ Developmental: >640 mg/m ³ .	(Murray <i>et al.</i> , 1979; TSCATS, 1992)
Oral (drinking water)	Gravid rats (Sprague-Dawley) imbibing 200 mg/L (approx. 40 mg/kg/day) for gd 6-15.	Maternal: >200 mg/L Fetal: >200 mg/L Developmental: >200 mg/L	(Murray <i>et al.</i> , 1979; World Health Organization, 1990) (191,96)
Oral (drinking water)	Rats (Sprague-Dawley) imbibing 0.15 or 110 mg/L VDC in drinking water for 2 months prior to and during pregnancy.	Developmental effects (total cardiac anomalies) at both dose levels.	(Dawson <i>et al.</i> , 1993)

^aCharles River CD strain rats are Sprague Dawley strain.

^bLow number of fetuses available due to high mortality in dams and low fertility index in all groups, including controls.

6.8 Immunotoxicity (Tier 2)

A guideline immunotoxicity study of VDC has not been undertaken; however, the potential immunotoxicity of VDC has been examined as part of a number of comprehensive repeated-dose toxicity studies. This has included the histopathological evaluation of selected lymph nodes, thymus, spleen and bone marrow of rats, mice and dogs administered VDC via the oral or inhalation routes for subacute, subchronic and/or chronic periods (Prendergast *et al.*, 1967; Norris, 1977; Quast *et al.*, 1977; Gage, 1970; Quast *et al.*, 1986; Rampy *et al.*, 1977; Rampy *et al.*, 1978; Quast *et al.*, 1983; National Toxicology Program, 1982; Lee *et al.*, 1977; DFG, 1985). In addition, Ban *et al.* (1998) utilized VDC as a model nephrotoxic and hepatotoxic compound to investigate the relationship of tissue damage and indirect immunosuppressive effects on cells of the immune system. Liver and kidney toxicity, serum concentrations of macrophage released cytokines tumor necrosis factor alpha (TNF- α) and interleukin-6 (IL-6), and sera antibody forming cell and natural killer cell assays were conducted in mice administered toxic dosages of VDC. It was concluded that the observed immunosuppressive potential of sera from these mice was related to tissue damage and increased serum TNF- α and IL-6 levels.

6.9 Metabolism and Pharmacokinetics (Tier 2)

The metabolism and pharmacokinetics of VDC has been extensively studied in rats dosed via oral or inhalation routes and *in vitro* using tissue fractions from a number of species, including humans (see Text Table 6.9.1). VDC is rapidly absorbed from the digestive or respiratory tracts, is extensively metabolized at lower dosages/exposures and excreted primarily via urine via saturable metabolic pathways. With increasing dosages/exposures a significant portion of absorbed VDC is eliminated as parent

material via exhalation. In general, nearly all absorbed VDC in treated rats is eliminated within 24-48 hours postdosing. Urinary metabolites and a variety of *in vitro* metabolism study findings have characterized the metabolism of VDC as epoxidation followed by spontaneous rearrangement and metabolism to chloroacetic acid. Subsequent conjugation of these products with glutathione provides the major detoxification pathway for VDC and its metabolites and the source of most nonvolatile excretory products.

Text Table 6.9.1. Metabolism and/or Pharmacokinetic Studies on VDC,

Study	Design	Key Findings	Reference
Oral Metabolism, Distribution and Pharmacokinetics	Rats (fed and fasted male Sprague-Dawley) administered 1 or 50 mg/kg ¹⁴ C-VDC and collection of excretion and tissue ¹⁴ C data, and urinary metabolite identification.	VDC well absorbed from GI tract with extensive metabolism (<3% eliminated unchanged) at low dosage. Saturation of metabolism was evident at the high dosage which was exacerbated by fasting (19% in fed; and 29% in fasted eliminated unchanged). Primary route of excretion via urine within 24 hours as 4 metabolites suggesting epoxidation followed by further oxidation and glutathione conjugation as a major route of metabolism.	(McKenna <i>et al.</i> , 1978)
Oral, Intravenous and Interperitoneal Metabolism and Excretion Kinetics	Rats (male Wistar) administered 0.5 or 350 mg/kg ¹⁴ C-VDC via intragastric or i.p. routes or 0.5 mg/kg via i.v. route followed by collection of excretion and tissue bound ¹⁴ C data, and urinary metabolite identification. Metabolism of putative metabolites was also examined.	Extensive hepatic metabolism evidenced by <1% p.o. and 12% i.p. eliminated unchanged while 80% i.v. eliminated at low dosage. Saturation of metabolism was evident at the high dosage with 67% p.o. and 91% i.p. eliminated unchanged. Urinary excretion products suggesting epoxidation followed by further oxidation and glutathione conjugation as a major route of metabolism.	Jones and Hathway, (1978)
Inhalation Metabolism, Distribution and Pharmacokinetics	Rats (fed and fasted male Sprague-Dawley) exposed to 40-800 mg/m ³ (10 or 200 ppm) ¹⁴ C-VDC for 6 hours and collection of excretion and tissue ¹⁴ C data, and urinary metabolite	Inhaled VDC well absorbed with extensive metabolism with <2% eliminated unchanged at 40 mg/m ³ (10 ppm) and 4-8% at 800 mg/m ³ (200 ppm) following exposure. Primary route of excretion via urine within 24 hours as 2 primary metabolites suggesting	(McKenna <i>et al.</i> , 1978)

	identification.	epoxidation followed by further oxidation and glutathione conjugation as a major route of metabolism. Fasting had no effect at 10 ppm but resulted in higher body burden and liver histopathology at 800 mg/m ³ (200 ppm).	
Oral and Intravenous Pharmacokinetics in Blood.	Rats (fed and fasted male Sprague-Dawley) administered 10-100 mg/kg VDC via i.v. or oral gavage and blood kinetic parameters determined.	Orally administered VDC well absorbed giving similar blood kinetics and AUC as following i.v. dosing. Blood half-lives of VDC ranged from 42 to 138 minutes with higher values observed with increasing dosage, oral administration and fed state (p.o. only). Elimination from blood occurred in a bi- (p.o.) or tri- (i.v.) phasic manner.	(Putcha <i>et al.</i> , 1986)
Inhalation Uptake and Excretion and Blood Pharmacokinetics.	Rats (anethetized and tracheostomized male Sprague-Dawley) exposed to 100-1200 mg/m ³ (25-300 ppm) VDC for 3 hours followed by a 30 minute additional collection period. Exhalation and venous blood concentrations of VDC determined.	Rapid absorption reaching steady state exhalation and blood concentrations within 45 minutes at ≤600 mg/m ³ (≤150 ppm) exposure. Saturation kinetics observed over time at 600 mg/m ³ (150 ppm) and 1200 mg/m ³ (300 ppm) clearly saturating exposure level.	(Dallas <i>et al.</i> , 1983)
Significance of Detoxification Pathways.	Rats (fasted male Holtzman and Fischer 344 rats) pretreated with a variety of agents known to inhibit specific Phase II enzymes used to establish LC50 values and metabolism rate constants for VDC.	Established significance of glutathione detoxification pathway(s) in metabolism of VDC and ruled out major involvement of epoxide hydrolase.	(Anderson <i>et al.</i> , 1980)
Physiologically – Based Pharmacokinetic Model	Developed computerized model to predict pharmacokinetic behavior of VDC in animals, including	Successfully predicted blood, tissue, exhaled VDC and liver GSH levels as a function of dose and route of administration. Explains “complex mortality curves	(D’Souza and Anderson, 1988)

	humans.	seen with VDC". Predicts blood half-life dependent on reequilibration of VDC from fat rather than representative of metabolism rates.	
Relative Activation Potential of Halogenated Ethylenes	Formulation of generalized mechanism based upon comparative biological activity of haloethylenes based upon chemical reactivity of halooxiranes.	Potential genotoxicity and oncogenicity of VDC represents a balance between inherent chemical reactivity and stability of epoxide metabolite. Concluded assymmetric haloethylenes more active than symetric (vinylchloride~vinylfloride>vinylidene floride>VDC).	(Henschler, 1977, Bolt et al, 1982)

6.10 Carcinogenicity (Tier 3)

Numerous independent studies evaluating the potential carcinogenicity of inhaled or orally administered VDC have been conducted in both sexes of rats, mice, and hamsters. Studies were conducted prior to GLP requirements and extensive experimental designs consistent with modern guideline are not available for most. The findings of several bioassays have been published in peer-reviewed journals. As shown in Text Table 6.10.1, a relatively wide range of dosing or exposure regimens has been employed. In general, no reproducible tumorigenic response has been reported following chronic oral or inhalation exposure to VDC. Indeed, the IRIS VDC document concludes "no evidence of carcinogenicity by the oral route of exposure" for ingested VDC and that the weight of evidence "is not sufficient to justify deriving an inhalation unit risk" for inhaled VDC (IRIS, 2002).

Of the approximately 18 bioassays conducted on the potential carcinogenicity of VDC, only the results of two studies have revealed an increased incidence of a particular tumor type. In an inhalation study conducted concurrent with a carcinogenicity study on vinyl chloride, Lee *et al.* (1977; 1978) reported that several VDC-exposed rats and mice had hemangiosarcomas, a tumor type characteristically produced by vinyl chloride. The latter factor plus the lack of subsequent confirmation in other bioassays in either species, has led to the assertion that cross contamination between the two studies had occurred (DFG, 1985). In another inhalation study, Maltoni *et al.* (1984; 1977; 1977) reported an excess incidence of kidney tumors in male mice chronically inhaling a relatively high concentration of VDC vapor. As discussed by the DFG Gesundheitsschaedliche Arbeitsstoffe, (1985), it has been suggested that an impurity in the VDC used, dichloroacetylene at a concentration of 20 ppm and a known renal carcinogen, may have contributed to the results observed. In addition, the metabolic activation of VDC to a potentially reactive compound has been reported by Speerschnieder and Dekant (1994) to occur primarily only in male mice and not females, rats or humans. Finally, VDC was found to function as an initiator of skin papillomas in a female mouse dermal initiation-promotion tumorigenesis assay but not a complete dermal carcinogen in studies conducted by Van Duuren *et al.* (1979).

Text Table 6.10.1. Carcinogenicity Studies on VDC.

Study	Design	Results	Reference
Inhalation	Rats (M&F Sprague-Dawley) exposed to 40-604mg/m ³ (10-150 ppm) 4 hours/day, 4-5 days/week, for 12 months and held until spontaneous death.	No treatment-related increases in incidence of tumors.	(DFG, 1985; Maltoni <i>et al.</i> , 1984; Maltoni, <i>et al.</i> , 1977; Maltoni, 1977)
Inhalation	Rats (M&F CD) exposed to 222 mg/m ³ (55 ppm) 6 hours/day, 5 days/week, for 12 months. Likely indeterminate exposure to vinyl chloride.	No treatment-related increases in incidence of tumors [hemangiosarcomas, characteristic tumor type for vinyl chloride, observed in a few rats] ^a .	(DFG, 1985; Lee <i>et al.</i> , 1977; Lee <i>et al.</i> , 1978; World Health Organization, 1990)
Inhalation	Rats (M&F Sprague-Dawley) exposed to 40-100 (10-25 ppm) or 160-300 mg/m ³ (40-75 ppm) 6 hours/day, 5 days/week, for 17 months and held a further 6 months.	No treatment-related increases in incidence of tumors.	(DFG, 1985; Rampy <i>et al.</i> , 1977; Rampy <i>et al.</i> , 1978; Quast <i>et al.</i> , 1983; World Health Organization, 1990)
Inhalation	Rats (M&F Wistar) exposed to 300-810 mg/m ³ (75-100 ppm) 4 hours/day, 5 days/week, for 12 months and held until spontaneous death. Also a group exposed to 1600 mg/m ³ (200 then 100 ppm) for 5 months then 810 mg/m ³ under same regimen.	No treatment-related increases in incidence of tumors.	(DFG, 1985; Viola and Caputo, 1977; World Health Organization, 1990)
Inhalation	Rats (M&F Sprague-Dawley) exposed to 400 mg/m ³ (ppm) 7 hours/day, 5 days/week, <i>in utero</i> (gd 12) or as weanlings and subsequently for 24 months.	Increase in total malignant tumors and leukemias; however, no statistical evaluation nor historical control data presented.	(Cotti <i>et al.</i> , 1988)
Inhalation	Mice (M&F Swiss)	Increase incidence	(DFG, 1985; Maltoni

	exposed to 40-100 mg/m ³ (10-25 ppm) 4 hours/day, 4-5 days/week, for 12 months and held until spontaneous death. Additional group exposed to 200 mg/m ³ (50 ppm) for only 4 days.	of kidney adenocarcinomas in 100 and 200 mg/m ³ males ^a .	<i>et al.</i> , 1984; Maltoni <i>et al.</i> , 1977; Maltoni, 1977)
Inhalation	Mice (M&F CD-1) exposed to 220 mg/m ³ (55 ppm) 6 hours/day, 5 days/week, for up to 6 months and held an additional 12 months.	No treatment-related increases in incidence of tumors.	(DFG, 1985; Hong <i>et al.</i> 1981)
Inhalation	Mice (M&F CD-1) exposed to 222 mg/m ³ (55 ppm) 6 hours/day, 5 days/week, for 12 months. Likely indeterminate exposure to vinyl chloride.	No treatment-related increases in incidence of tumors [hemangiosarcomas , characteristic tumor type for vinyl chloride, observed in a few mice] ^a .	(DFG, 1985; Lee <i>et al.</i> , 1977; Lee <i>et al.</i> , 1978; World Health Organization, 1990)
Inhalation	Hamsters (M&F Chinese) exposed to 100 mg/m ³ (25 ppm) 4 hours/day, 4-5 days/week, for 12 months and held until spontaneous death.	No treatment-related increases in incidence of tumors.	(DFG, 1985; Maltoni <i>et al.</i> , 1984; Maltoni <i>et al.</i> , 1977; Maltoni, 1977; TSCATS, 1992)
Oral (drinking water)	Rats (M&F Sprague-Dawley) imbibing 50-200 mg/L VDC for 24 months.	No treatment-related increases in incidence of tumors.	(DFG, 1985; Rampy <i>et al.</i> , 1977; Rampy <i>et al.</i> , 1978; Quast <i>et al.</i> , 1983; World Health Organization, 1990)
Oral (drinking water)	Rats (M&F Sprague-Dawley) imbibing mg/L (5-12 to 16-40 mg/kg/day) VDC for 24 months.	No treatment-related increases in incidence of tumors.	(TSCATS, 1978)
Oral (gavage)	Rats (M&F Sprague-Dawley) administered 0.5-20 mg/kg/day VDC in olive oil 4-5 times/week for 12 months and held	No treatment-related increases in incidence of tumors.	(DFG, 1985; Maltoni <i>et al.</i> , 1984; Maltoni <i>et al.</i> , 1977; Maltoni, 1977; TSCATS, 1992)

	until spontaneous death.		
Oral (gavage)	Rats (M&F F344/N) administered 1 or 5 mg/kg/day VDC in corn oil 5 times/week for 24 months.	No treatment-related increases in incidence of tumors.	(DFG, 1985; National Toxicology Program, 1982)
Oral (gavage)	Mice (M&F B6C3F1/N) administered 2 or 10 mg/kg/day in corn oil for 23 months.	No treatment-related increases in incidence of tumors.	(DFG, 1985; National Toxicology Program, 1982)
Dermal (skin paint)	Mice (F ICR/Ha Swiss) administered 121 mg/animal in acetone 3/week for life.	No treatment-related increases in incidence of tumors	(DFG, 1985; Van Duuren <i>et al.</i> , 1979; World Health Organization, 1990)
Subcutaneous Injection	Mice (F ICR/Ha Swiss) administered 2 mg/animal in trioctanoin once/week for 548-636 days.	No treatment-related increases in incidence of tumors	(DFG, 1985; Van Duuren <i>et al.</i> , 1979; World Health Organization, 1990)
Initiation-Promotion	Mice (ICR/Ha Swiss) administered one dermal dose of 121 mg/animal followed by 0.005 mg/animal phorbol ester 3/week for life.	Increased incidence of skin papillomas but no distal site tumors.	(DFG, 1985; Van Duuren <i>et al.</i> , 1979; World Health Organization, 1990)

^aSource and/or significance of tumors has been questioned.

6.11 Neurotoxicity (Tier 3)

The potential neurotoxicity of VDC has been examined in animals under a variety of study designs involving several different species of test animals, routes of administration and duration of dosing. While not encompassing a complete set of parameters examined in guideline neurotoxicity studies, a number of subacute, subchronic and/or chronic studies have involved a careful neurotoxicity evaluation. These studies have included the antemortum examination of physical and behavioral characteristics and thorough post-mortem gross and histopathological evaluations of central and peripheral nervous tissues. There has been no reproducible indication of a direct neurotoxic effect of VDC in test species, including neonates.

6.12 Developmental Neurotoxicity (Tier 3)

An all-encompassing study involving the dosing of a test species in utero and continuing at an MTD level as young neonates, extensive histopathological evaluation of neonate central and peripheral nervous tissues, and extensive behavioral evaluation of pups has not been conducted on VDC. However, much of the various parts of a developmental neurotoxicity study have been conducted as portions of numerous developmental toxicity studies, a multigeneration reproduction study conducted by Nitschke *et al.* (1983), teratogenicity studies, and a developmental neurobehavioral examinations conducted by Short *et al.* (1977) on rat pups. No reproducible evidence of neurological tissue terata

have been observed in rats, mice or rabbits exposed *in utero* to VDC at maternally toxic dose/exposure levels over the gestation period covering a majority of organogenesis. Evidence of fetotoxicity such as lowered pup body weights and number or delayed ossification of certain bones observed at maternally toxic dose/exposure levels in developmental toxicity studies has not included any evidence of neurotoxicity. In addition, no evidence of neurotoxicity has been observed upon multiple generations of rats exposed to VDC *in utero*, during nursing and maturation in a reproduction study. And finally, the direct evaluation of potential developmental neurological effects of VDC has been provided in a study by Short *et al.* (1977) in which a variety of behavioral/activity tests of rat pups exposed *in utero* to maternally toxic levels of VDC were conducted. Evaluations started from postnatal day 1 and continued through postnatal day 21. Significantly, the conclusion of the study was that “no problems with neural development, as measured by behavioral parameters, were observed”.

6.13 Other Relevant Information (no requirement)

There have been at least two epidemiology studies that examined cancer risks of VDC workers (Ott *et al.*, 1976; Theiss *et al.*, 1977). The Ott *et al.* (1976) study examined the cancer rates of 138 workers with measured levels of VDC where vinyl chloride was not used a copolymer. Exposure monitoring was done on all workers from 1944 onward and the average time weight exposures range from 70 ppm in the fiber production area to less than 5 ppm for laboratory technicians. Although the study size was small, there was no increase risk of death (SMR=0.7, 95%CI 0.2-1.6) or cancer (SMR=0.9, 95% CI 0.0-5.1). Theiss *et al.* (1977) examined the mortality rates of 629 workers exposed to VDC and both cancer rates and death rates were at expected levels. The study of Ott *et al.* also examined clinical blood chemistries, blood pressure and pulmonary function for exposed workers and matched controls. No significant differences were observed between the groups. While the epidemiology data on VDC are limited, there is no indication of adverse health effects from exposure.

6.14 Hazard Assessment Summary

There have been no reproducible findings suggesting a unique sensitivity of young animals to the toxic effects of VDC with the possible exception of acute exposure lethality. Anderson and Jenkins (1977) have reported that leaner, presumably younger, rats were more susceptible than heavier, presumably older, rats to lethal dosages of VDC. The authors suggested that this latter finding was related to increased metabolic activity in weanling rats relative to older animals; however, results could also be explained based upon effects of body fat upon distribution of VDC. A less reliable purported age-related effect of VDC has been the reported finding by Dawson *et al.* (1990; 1993). These latter authors reported an increase in total cardiac anomalies in rats exposed to VDC *in utero* via drinking water administered dams or via direct infusion into the gravid uterus of rats by implanted osmotic pump. However, no cardiac anomalies have been reported in several Guideline-quality studies employing maternally toxic dosages of VDC, nor have similar finding by this group with trichloroethylene been reproduced by two independent laboratories at maternally toxic dosages (Fisher *et al.*, 2001; Carney *et al.*, 2001). Further, the findings of Dawson *et al.* have been criticized by the IRIS Peer Review Workshop (2001) for lack of dose-response, high control rates of malformations, lack of specificity and a number of quality control problems. The EPA Integrated Risk Information System (IRIS, 2002) concludes that “the changes reported by Dawson *et al.* (1993) must be assumed at this point to represent variations in cardiac morphology that have little or no physiological consequence”.

Specific studies similar to those outlined in present day or proposed immunotoxicity, neurotoxicity and developmental neurotoxicity study guidelines have not been

undertaken for VDC. However, over a dozen studies have involved the repeated evaluation of treated test animals for clinical signs of toxicity and gross and histopathological evaluations of testes, ovaries, secondary sex organs, lymph nodes, thymus, spleen, central nervous system tissues, and peripheral nerves. No findings suggestive of a primary effect of VDC upon the immune or nervous systems have been reported, indicating a lack of potential VDC immunotoxicity or neurotoxicity. In addition, a study of potential behavioral effects of VDC upon rats exposed to vapor under a continuous exposure regimen *in utero* has revealed no indication of developmental neurotoxicity. Finally, studies of the metabolism of VDC in rats have revealed that the toxicity of VDC is dependent upon a balance between its activation and detoxification via saturable enzymatic pathways that can be influenced by the nutritional state, body size and sex of treated animals.

It is concluded that VDC has been adequately studied in laboratory tests designed to characterize the potential toxicity categories outlined in the VCCEP Program. Further testing would represent an unnecessary and possibly redundant evaluation of VDC. (Stott, W., 2002)

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6.15 Robust Summaries of Toxicology Studies

The IUCLID format has been utilized to present the robust summaries of the available mammalian toxicity data on VDC. As the IUCLID data set also contains data that are not relevant to the VCCEP, only Chapter 5, Mammalian Toxicity, has been included in Appendix C.

7. Risk Assessment

7.1 Risk Receptors

Risk estimates have been obtained for both children and adults for four exposure scenarios. These scenarios are inhalation of ambient and indoor air, ingestion of drinking water, and ingestion of food that has contacted PVDC containing film. The child receptor for the ambient air and drinking water assessments was chosen based upon the age categories recommended in the CalEPA Guidance for Stochastic Analysis and the USEPA Exposure Factors Handbook. One age category (0 to 12 years) with no sex distinction was obtained by CalEPA for body weight normalized inhalation rates. The drinking water ingestion pathway used the USEPA Exposure Factors Handbook to give age specific consumption data for children. A separate drinking water exposure calculation for infants less than one year old was included. The drinking water exposures for 18 years of childhood were calculated to give an estimate of childhood exposure and risk.

7.2 Hazard Benchmarks

Primary guidance for obtaining health protective benchmarks for use in risk calculations was obtained from the USEPA IRIS data for 1,1-dichloroethylene (USEPA 2000). In addition the CalEPA Chronic Inhalation Reference Exposure Level derived in the Chronic Toxicity Summary for 1,1-Dichloroethylene (CalEPA 2000a) was used together with the IRIS RfC for ambient air scenarios.

The USEPA Reference Dose for chronic oral exposure, RfD, and the USEPA reference concentration for chronic inhalation exposure, RfC, provide the primary values for the evaluation of the exposure scenarios. These are defined as “safe” exposure levels under the assumption that thresholds exist for certain toxic effects. IRIS evaluates the potential human carcinogenicity of the substance independently of the evaluation of toxic effects following chronic exposure that are presumed to have thresholds.

As described in IRIS, “In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime.”

The RfC is described in similar terms, “The inhalation Reference Concentration (RfC) is analogous to the oral RfD and is likewise based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. The inhalation RfC considers toxic effects for both the respiratory system (portal of entry) and for effects peripheral to the respiratory system (extrarespiratory effects). ... In general, the RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily inhalation exposure of the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime.”

The critical effect identified by the USEPA for both inhalation and oral chronic exposures and by the CalEPA for inhalation exposure was liver toxicity. The principal study identified by USEPA for chronic oral exposure was Quast et al. (1983), that for chronic inhalation exposure was Quast et al. (1986). The California EPA identified Pendergast et al. (1967) as the principal study for chronic inhalation exposure. The USEPA and California guidance levels were obtained by applying health protective uncertainty factors (UF) to the no observed adverse effect level, NOAEL, or a benchmark concentration or dose level, BMCL or BMDL, for the critical effect obtained from animal tests.

The USEPA IRIS RfD is based upon a 2-year chronic toxicity and carcinogenicity study in rats (Quast et al. 1983). Male rats had a NOAEL of 10 mg/kg/day and female rats had a NOAEL of 9 mg/kg/day. The IRIS RfD was obtained by calculating a BMDL₁₀, and applying interspecies and intraspecies uncertainty factors of 10 and 10. The BMDL₁₀ obtained was 4.6 mg/kg/day. Dividing this by the uncertainty factor of 100 gives the IRIS RfD of 0.05 mg/kg/day (50 µg/kg/day).

The USEPA IRIS RfC is based upon an 18 month, 6 hour per day exposure using rats (Quast et al. 1986). Male rats had a NOAEL of 300 mg/m³ (75 ppm) and female rats a LOAEL of 100 mg/m³ (25 ppm). The IRIS RfC was obtained by calculating a BMCL₁₀, the 95% lower confidence limit on the extrapolated concentration where a minimal response (10%) occurs, adjusting the BMCL₁₀ for continuous exposure and applying interspecies and intraspecies uncertainty factors of 3 and 10. The BMCL₁₀ obtained was 39 mg/m³, adjusting for continuous exposure this is 6.9 mg/m³. Dividing this by the uncertainty factor of 30 gives the IRIS RfC of 0.2 mg/m³ (200 µg/m³).

The California noncancer chronic reference exposure level (REL) is based on a 90-day continuous exposure experiment with Guinea pigs (Pendergast et al. 1967). The NOAEL for the critical effect was 20 mg/m³. Applying uncertainty factors of 10 for subchronic to chronic extrapolation, 10 for intraspecies variability, and 3 for interspecies variability gives a net uncertainty factor of 300. Dividing the NOAEL by the UF gives the chronic inhalation REL of 70 µg/m³.

To add exposures from different routes they are put on a common basis. Since VDC is relatively well absorbed following inhalation, and since VDC at chronic exposure concentrations does not have a portal of entry critical effect, inhaled concentration was converted to dose assuming 100% absorption and the daily inhalation volumes normalized to body weight appropriate to the age group under consideration and available in published guidance (CalEPA 2000b). This gives both inhalation and oral doses in units of mass of VDC/body weight/day allowing aggregation over these routes by addition of the doses. The aggregate dose is then compared to the RfD derived from the critical effect, liver toxicity.

Since the weight of evidence evaluation in IRIS concludes that no exposure routes have data that justifies quantitative estimates of carcinogenic risks from those exposures, no numerical estimates of carcinogenic risk are presented. This is consistent with the IRIS weight of evidence characterization of the data relevant to the evaluation of the human carcinogenicity of VDC which concludes:

"EPA concludes that the results of kidney tumors in one sex and one exposure in a single species of rodents are too limited to support an exposure-response assessment."

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7.3 Margins of Safety for Childhood Exposure to VDC

The ratio of the hazard benchmark to the exposure gives an estimate of the risk associated with that exposure. Since the reference dose, RfD, was derived by the incorporation of uncertainty factors to account for the differences between the experimental exposure of rodents and the scenario of interest, the potential exposure of humans (the ratio using the RfD) is shown as a Margin of Safety in Tables 7.3.1 and 7.3.2 on the following page. The direct comparison of the exposure to the hazard benchmark without the incorporation of uncertainty factors, is shown as the Margin of Exposure in the same Tables on the following page. Since no scaling for the ratio of the body weights or body surface areas has been included, these values differ by a factor of 100, the net uncertainty factor, within the precision of the rounded values. As noted in the title, the margins of safety presented in Tables 7.3.1 and 7.3.2 are calculated for children. While they are not included in the table, since the corresponding adult and lifetime exposures are marginally less than those for children, the margins of safety for prospective parents are even greater than those noted for children.

In Table 7.3.1, the margin of safety for the typical exposure for each route is at least three orders of magnitude and the margin of safety for the aggregate exposure is also three orders of magnitude. Since margins of safety greater than one are generally viewed as providing a reasonable expectation of no adverse effect, the typical childhood aggregate exposure to VDC is reasonably expected to be inconsequential.

In Table 7.3.2, the margin of safety for the high end exposure for each route is at least two or three orders of magnitude. The margin of safety for the sum of these unlikely exposures is greater than two orders of magnitude. Improbable high end childhood aggregate exposure to VDC is reasonably expected to be inconsequential.

Table 7.3.1 Typical Childhood Exposure - Margin of Safety

	Central Tendency Exposure $\mu\text{g}/\text{kg}/\text{day}$	Margin of Safety RfD ^a /Exposure	Margin of Exposure BMDL ₁₀ ^b /Exposure
Ambient Air (20% of time) ^g	0.024 ^c	2100	190,000
Indoor Air – Carpet (80% of time) ^g	0.023 ^d	2200	200,000
Drinking Water	0.008 ^e	6250	575,000
Oral - Food Wrap	0.010 ^f	5000	460,000
Total	0.065	770	77,000

^a The RfD is 50 $\mu\text{g}/\text{kg}/\text{day}$ (USEPA IRIS 2002).

^b The Benchmark Dose Limit for liver toxicity in the rat is 4600 $\mu\text{g}/\text{kg}/\text{day}$ (USEPA IRIS 2002).

^c 20% of the median value overestimate for children aged 1 to 18 years (Fontaine 2002a).

^d 80% of the value obtained using the maximum air concentration of 0.063 $\mu\text{g}/\text{m}^3$ (Fontaine 2002b) and the mean inhalation rate of children aged 1 to 12 years of 0.441 $\text{m}^3/\text{kg}/\text{day}$ (CalEPA 2000).

^e The median value overestimate for children aged 1 to 12 years (Fontaine 2002c).

^f Estimated using 1 kg of food only ingestion per day per child.

^g Jenkins, Overview: California Indoor Exposures and Risk. Abstract Presented at Indoor Air Quality: Risk Reduction in the 21st Century

Table 7.3.2 High End Childhood Exposure - Margin of Safety

	High End Exposure $\mu\text{g}/\text{kg}/\text{day}$	Margin of Safety RfD ^a /Exposure	Margin of Exposure BMDL ₁₀ ^b /Exposure
Ambient Air (20% of time) ^g	0.072 ^c	690	64,000
Indoor Air – Carpet (80% of time) ^g	0.027 ^d	1900	170,000
Drinking Water	0.014 ^e	3600	330,000
Oral - Food Wrap	0.0375 ^f	1300	120,000
Total	0.15	330	31,000

^a The RfD is 50 $\mu\text{g}/\text{kg}/\text{day}$ (USEPA IRIS 2002).

^b The Benchmark Dose Limit for liver toxicity in the rat is 4600 $\mu\text{g}/\text{kg}/\text{day}$ (USEPA IRIS 2002).

^c 20% of the 95th %-tile overestimate for children aged 1 to 18 years (Fontaine 2002a).

^d 80% of the value obtained using the maximum air concentration of 0.063 $\mu\text{g}/\text{m}^3$ (Fontaine 2002b) and the 90th %-tile inhalation rate of children aged 1 to 12 years of 0.5405 $\text{m}^3/\text{kg}/\text{day}$ (CalEPA 2000).

^e The 95th %-tile overestimate for children aged 1 to 12 years (Fontaine 2002c).

^f Estimated using 3 kg of food and drink ingestion per day per child (Fontaine 2002d).

^g Jenkins, Overview: California Indoor Exposures and Risk. Abstract Presented at Indoor Air Quality: Risk Reduction in the 21st Century.

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8. Data Needs Assessment

Just as “Risk” for any compound is determined by the interaction of “Hazard” and “Exposure”, the evaluation of data adequacy in meeting the objectives of VCCEP requires the examination of both hazard data and exposure data, including projected future exposure potential. These databases are not exclusive of each other. A lack of potential exposure of a specific population may negate the need for a very focused examination of a particular hazard endpoint. Conversely, the lack of a specific hazardous property may negate need for extensive exposure monitoring of a specific population to a compound. Modeling of worst case, generally unrealistic, scenarios of exposure for a specific population such as children may further place the potential risk posed by a chemical in perspective. **When the hazard and exposure databases for vinylidene chloride (VDC) were examined and utilized to model risk, it was concluded that no further exposure monitoring or hazard evaluation studies were warranted given present and anticipated future use conditions.**

The potential for exposure to VDC has been extremely well characterized. The review undertaken included analyses of the VDC life cycle and customer surveys as well as detailed ambient air, drinking water and relevant end-use applications assessments. A relatively clear picture of potential exposure of humans, and in particular children, to VDC has emerged, both for present and anticipated future uses. Potential sources of exposure are limited and expected to continue to decline as they have for a number of years. Applications are largely industrial-based “closed systems” polymer production operations. The few consumer applications that exist such as use in carpet backing polymers and film wraps, have extremely limited potential for exposure due to processing practices, for example the oven drying of carpets, prior to consumer contact. Also, releases from manufacturing and processing operations are continuing to decline as so-called “fugitive emissions” are brought under tighter control. Finally, one of the greatest potential environmental sources of VDC is via the degradation of 1,1,1-trichloroethane. This source of VDC, however, was phased out of production in the U.S. by 1995 under the Montreal Protocol.

Environmental monitoring data support the general lack of exposure of humans via the ambient environment. Of the nearly 22,000 air samples reportedly analyzed, including industrial sites known to be utilizing VDC, only 10% have had detectable levels of this chemical. In addition, only 1.5% of the approximately 64,000 water system samples reportedly analyzed have contained detectable levels. A large majority of air and water samples with detectable levels were found over a decade ago and had median values of only 0.1 $\mu\text{g}/\text{m}^3$ and 1.2 ppb, respectively. Additional, yet potentially flawed, personal air sampling data has been provided as part of the TEAM study that was cited by EPA in selecting VDC for inclusion in VCCEP. This latter study consisted of 1085 personal air samples from New Jersey over three sampling periods (seasons) but did not include children and were weighted toward industrial workers and smokers. North Carolina and

North Dakota sites were also included in the survey but VDC findings were not judged to be "prevalent" in samples from these latter two sites. The flawed sampling techniques used in addition to the lack of control for generation of VDC from other chlorinated hydrocarbons make the use of these data questionable. Only 6-11% of the population monitored had samples containing detectable VDC levels.

In addition to exposure information, an extensive hazard database has been accumulated for VDC. Toxicity has been extensively studied in a variety of assays and in a number of different species of test animals. Data has been generated on categories listed in all three Tiers of the VCCEP. The age and sources of many of these studies have ensured a heterogeneous database containing studies of varying sophistication and range. However, in many cases, multiple studies are available that individually or collectively provide a complete assessment of a particular VCCEP hazard category. Conversely, numerous studies have provided data that is applicable to more than one VCCEP category, for example the evaluation of gonads, nervous and immune system tissues in repeated-dose toxicity studies providing assessments of potential reproductive toxicity, neurotoxicity and immunotoxicity, respectively. Age-dependent effects have specifically been examined as part of developmental and reproductive toxicity studies. In addition, evaluation of age-specific sensitivity to potential neurotoxicity of VDC has been examined in growing rat pups. These studies have not demonstrated any age-related sensitivity to VDC toxicity. Further testing to provide comprehensive evaluations of those few remaining categories of tests listed in VCCEP specifically targeted for evaluation in young animals would be dependent upon evidence of significant potential exposure of children. Further testing for hazard assessment alone, in the absence of substantiated VDC exposure would represent an unwarranted expenditure of economic and test animal resources.

In an effort to provide estimates of potential exposure of children to VDC, exposure and hazard information were distilled to generate a focused risk assessment for children. Four potential sources of VDC exposure of children aged one to eighteen were considered; ambient air, the backing used in some indoor carpeting, drinking water, and migration from plastic wraps into food. Very conservative estimates of exposure were utilized. Only air samples having detectable levels of VDC, <10% of the samples collected, were used to define potential exposure. Residual (unreacted) VDC content in liquid latex applied to carpets was used, ignoring the % market share of VDC-containing carpets and the significant loss of volatile chemicals that occurs during oven drying of carpets. In the water assessment, it was assumed that all drinking water contains at least the limit of detection levels of VDC in well water analyses. Finally, the maximum levels of monomer in food wraps was assumed in the polymer food wrap assessment. Despite this, estimated exposures from each potential source or as an aggregate exposure, were several orders of magnitude less than the EPA identified acceptable daily intake of VDC (RfD). When compared to minimally toxic levels defined by animal studies and converted to Benchmark Dosages (BMDL), even worst case aggregate exposure scenarios were 3-4 orders of magnitude lower. It is beyond reasonable expectations that an age-related sensitivity can exceed this safety margin.

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