



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460

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OFFICE OF  
PREVENTION, PESTICIDES AND  
TOXIC SUBSTANCES

Ms. Sally Kokke-Hall  
EH&S Global Product Leader  
2020 Dow Center  
Midland, MI 48274

Dear Ms. Kokke-Hall:

Thank you for coordinating Dow Chemical Company's (Dow) sponsorship and assessment activities regarding vinylidene chloride (VDC) in EPA's Voluntary Children's Chemical Evaluation Program (VCCEP). EPA truly appreciates Dow's contributions to this program.

This letter is to inform Dow of EPA's VCCEP Tier 2 Data Needs Decision for vinylidene chloride (VDC). In formulating this decision, EPA has considered all available information including assessments provided by Dow and the results of the VCCEP VDC Peer Consultation. EPA concurs that there are sufficient Tier 1 toxicology and exposure information on VDC to characterize risks to children. EPA has not identified any VCCEP Tier 2 data needs for VDC which is consistent with the conclusions of the Peer Consultation. EPA did, however, note a few issues related to transparency and clarity in the initial Tier 1 assessment. These concerns have been generally addressed by the submission of supplemental information by Dow dated January 19, March 7, and May 23, 2005. EPA's Data Needs Assessment document will be posted to the VCCEP website, along with this decision letter, so that other stakeholders are informed of the status of this review. EPA notes that this decision is specific for VDC and does not set a precedent for future VCCEP cases.

Please contact Linda Gerber, the Acting Associate Director of the Chemical Control Division of EPA's Office of Pollution Prevention and Toxics, if you have any questions or concerns associated with this Data Needs Decision. Ms. Gerber can be reached at (202) 564-3452.

Sincerely,

A handwritten signature in black ink, appearing to read "Charles M. Auer".

Charles M. Auer  
Director, Office of Pollution Prevention  
and Toxics

Enclosure

**VOLUNTARY CHILDREN'S CHEMICAL  
EVALUATION PROGRAM:  
DATA NEEDS DECISION DOCUMENT  
OF VINYLIDENE CHLORIDE**

Prepared By  
Risk Assessment Division (7403M)  
Office of Pollution Prevention & Toxics  
June 20, 2005

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## Preface

Chemicals of potential concern to children's health are the subject of evaluation in the pilot Voluntary Children's Chemical Evaluation Program (VCCEP). VCCEP was developed to ensure that there are adequate publicly available data to assess the impact that industrial chemicals may have on children.

In August 1999, OPPT announced the initiation of a process in which it sought stakeholder input on all aspects of the VCCEP. OPPT held three public meetings and took comments on possible designs for a voluntary program. After considering all the comments of interested stakeholders, the pilot VCCEP was announced in a *Federal Register* notice on December 26, 2000. In the notice, OPPT asked companies that produce and/or import 23 specific chemicals to volunteer to sponsor their evaluation in Tier 1 of a pilot of the VCCEP. Thirty-five companies and ten consortia responded and volunteered to sponsor 20 of the chemicals.

The ultimate objective of the VCCEP is to ensure that there are adequate toxicity and exposure information available to assess the potential risks to children. A tiered approach is being pursued to gather the information, with each subsequent tier, of the three tiers, including more complex toxicology and exposure studies. Information from all three tiers may not always be necessary to adequately characterize the risk to children. The sponsor develops a chemical assessment at each tier of analysis. The assessment includes four sections: a summary of the toxicology information, a summary of the exposure information, a risk characterization, and a data needs assessment. The data needs assessment discusses the need for additional data, which could be provided by the next tier, to fully characterize the risks the chemical may pose to children.

During the public stakeholder meetings, it was proposed that an outside group of scientific experts should have the opportunity to provide comments on the data needs portion of the assessments. The approach adopted involves convening a group of scientific experts with extensive and broad experience in toxicity testing and exposure evaluations, as well as expertise in the specific chemical, referred to as a Peer Consultation Panel. The sponsor provides the assessments to an outside third party who is responsible for seeking input through the Peer Consultation Panel. The outside third party develops a summary of the panel's opinions and makes it available to the sponsor and the public.

OPPT reviews the sponsor's assessment and develops a response to the sponsor specifically on the data needs assessment. The response focuses primarily on whether any additional information is needed to adequately characterize the potential risks to children. EPA's response is sent to the sponsor and made available to the public.

Additional information regarding the Voluntary Children's Chemical Evaluation Program is provided in Appendix A and is available at <http://www.epa.gov/oppt/chemrtk>.

## Introduction

In November, 2002 the Dow Chemical Company submitted its tier 1 assessment of Vinylidene Chloride (VDC) for the Voluntary Children's Chemical Evaluation Program (VCCEP). OPPT has reviewed the four components of the assessment, and where appropriate, had confirmed the accuracy of the toxicology and exposure information. EPA has recently independently reviewed the available toxicology information as part of its IRIS program. This assessment has been extensively peer reviewed and was published in June, 2002. In addition, EPA has reviewed a report of a peer consultation panel that provided comments on the assessment; this report is available at [www.tera.org](http://www.tera.org). Finally, EPA has reviewed additional information provided by the Dow Chemical Company in letters dated January 19, 2005, March 7, 2005, and May 23, 2005.

### 1.0 Summary of EPA Recommendations for VCCEP Tier 2 Data Needs

1. EPA agrees that all tier 1 exposure analyses have been conducted. For VCCEP, EPA does not recommend any tier 2 exposure studies.
2. EPA agrees that all tier 1 toxicology studies have been conducted. EPA also notes that most tier 2 toxicology studies have been conducted. EPA does not recommend additional tier 2 studies for VCCEP at this time.

### 2.0. Summary of Tier 1 Exposure Assessment

#### Production, Applications and Fate of VDC

The sponsor's assessment states that the potential for exposure to VDC has been well characterized and that potential sources of exposure are limited and are expected to continue to decline over time. At the present time VDC is produced solely for use as a chemical intermediate and the applications of VDC are largely industrial-based, closed-systems for polymer production operations. The sponsor concludes that there is extremely limited potential for consumer exposure because only low levels of VDC remain in the polymers. The assessment also states that one of the greatest potential environmental sources of VDC is the degradation of 1,1,1 - trichloroethane but notes that production of this chemical was phased out under the Montreal Protocol.

Non-confidential estimates of current production capacity are difficult to obtain because of the limited number of global producers. Dow is the only current U.S. producer.

The submission addressed the fate of VDC in groundwater, soil and air. Because of its physical properties, The sponsor concluded that VDC is expected to exist primarily in air rather than other environmental compartments. In air, VDC should be rapidly oxidized.

Potential sources of VDC exposure to children and the environment could come from production, processing, use and disposal of VDC or from degradation in the environment of higher chlorinated compounds to VDC. TRI releases for 2000 are provided. They show that most releases to the environment from the reporting facilities are to air.

The major application of VDC are as an intermediate in the production of polyvinylidene polymers, copolymer and terpolymers as well as the production of chloroacetylchloride and a hydrofluorocarbon (HFC236fa). The specific polymer applications identified that have relevance to children's exposure were PVDC latex for carpet backing and PVDC for food packaging. Polymer applications that The sponsor concluded did not have the potential for children's exposure were VDC-based latex for foil scrim kraft, VDC-containing latex for photographic film coating, PVDC for flame retardant fibers for clothing and PVDC/fluorinated copolymer applications on textile.

#### Occupational Exposure

NIOSH (NOES Survey 1082-1983, NIOSH 1989) estimated that 2,675 workers were exposed to vinylidene chloride (VDC) in the United States. Included are operators of equipment manufacturing, processing, and incorporating VDC into commercial products as well as maintenance workers, researchers, and others who might handle or work with VDC. In a 1983 EPA Health Assessment, VDC concentrations in monomer and polymer manufacturing plants were reported to be 90-100 ug/m<sup>3</sup> (22-25 ppb) and 25-50 ug/m<sup>3</sup> (6.2-12 ppb), respectively. Levels as high as 7,700 mg/m<sup>3</sup> (1,900 ppm) were found in a VDC-ethyl acrylate copolymer monofilament fiber production plant. The TWA exposure levels for different job categories in this same plant ranged from 6 to 70 ppm. The greatest likelihood for occupation air concentrations of VDC to exceed the NIOSH REL of 0.4 ppm or the ACGIH TLV of 5 ppm exists during transfer operations, sampling, and maintenance activities. In a letter dated March 7, 2005, the Dow Chemical Company provided a study entitled "Vinylidene Chloride: Developmental Toxicity Study Findings in Relation to Occupational Exposure." The study states 'measurements in production facilities are reported to be much lower than 5 ppm which was reconfirmed during industrial hygiene monitoring in 2001 and 2002.

#### Children's Exposure

Ten plausible exposure pathways (scenarios) were identified. Of the ten, four were selected for assessment. In a letter from The Dow Chemical Company dated May 23, 2005, rationale was provided as to why Dow did not preform assessment for these scenarios. The four that were selected are: inhalation of VDC in ambient air; ingestion of VDC in water due to its detection in groundwater and drinking water sources; ingestion of food that has been in contact with VDC containing polymer food wrap; and inhalation of VDC in residential indoor air from carpet backing emissions. In addition, an aggregate exposure scenario was included in the assessment. These four pathways and the aggregate exposure scenario are summarized below.

## 1. Ambient Air Exposure Pathway

The sponsor conducted a study to provide estimates of inhalation exposure to children in the United States to VDC in ambient air. A distribution of ambient air concentrations was obtained from the air toxics data archive maintained by USEPA and state air pollution control professionals. Nineteen monitoring programs in 19 states and the District of Columbia provided over 20,000 observations in the archive for VDC. The analyses found that 90% of the observations were non-detects and only 10% were detects. The sponsor reported that about half of the positive detections are less than  $0.1 \text{ ug/m}^3$  and that the largest reported concentration was  $69.4 \text{ ug/m}^3$ . The monitoring data records are dated from September 1981 to March 2000.

The exposure analysis was done using only positive detects. The non-detects were not used because the detection limits were not available in the archive. The study provided two different approaches for estimating the exposure for this pathway. In the first approach, a table was presented with ranges of ambient air concentrations along with the "exposures (ug/kg/day)" that would result for the 10<sup>th</sup>, mean and 90<sup>th</sup> percentile inhalation rates for a child. To calculate the exposures, the midpoint of each concentration range was used. In this study a child was defined as being between 0 and 12 years old. Results are also provided for adolescents and adults (i.e. greater than 12 years old) in a separate table. The highest result that was found was 41 ug/kg/day.

In addition, a Monte Carlo analysis was conducted which repeatedly sampled the air concentration distribution and a inhalation rate distribution (from a CalEPA guidance) for values according to their probability of occurrence. The product of the values was used to create a probability distribution of exposure. The probability associated with each exposure value was the ratio of the number of times that an exposure value occurred to the total number of exposure values calculated. The sponsor estimated childhood average daily exposures for 36 four month periods from age 0 to 12 years old. The four month averaging time was driven by considerations involving the monitoring data and was selected as a compromise. Tables were presented with exposure estimates from 100,000 childhood and lifetime simulations.

## 2. Drinking Water Exposure Pathway

The sponsor conducted a study to provide estimates of the distribution of drinking water exposures of children in the United States to VDC. An estimate of exposure to the general public is also provided. The distribution of drinking water concentrations was developed from the National Contaminant Occurrence Database (NCOD) which is maintained by EPA. The VDC data in the NCOD come from over 9,000 monitoring locations and represent about 65,000 observations. The monitoring locations are in 22 states plus the District of Columbia, Puerto Rico and the Virgin Islands. Groundwater sources accounted for 8,098 (88%) of the systems with 1.6 % of these having detectable levels of VDC. Surface water sources accounted for 1,043 of the systems and 4% of these had detectable levels of VDC. Groundwater sources under the direct

influence of surface water accounted for 37 of the systems and only one of these had a detectable level of VDC. The records in the NCOD dated from January 1984 to January 2001.

The sponsor used two approaches to estimating exposure to VDC in drinking water. In the first approach tables with ranges of water concentrations and "exposures" (ug/kg/day) for mean, 10<sup>th</sup> and 90<sup>th</sup> percentile water intakes for children less than 1 year old, for children ages 1 to 10, and for teenagers ages 11 to 20 were generated. The midpoint of each concentration range was used to estimate the exposures. The highest mean exposure was 3.3 ug/kg/day and the highest 90<sup>th</sup> percentile exposure was 7.5 ug/kg/day.

In the second approach, a Monte Carlo method was used to estimate exposures. Exposure estimates were generated by repeatedly sampling the concentration and water intake distributions. The water concentration was represented by sampling from all of the measured samples rather than using the concentration ranges. Exposures were estimated for children and adults, as well as lifetime exposures. The child's mean exposure estimated at 0.009 ug/kg/day and the highest exposure estimated at 0.4 ug/kg/day.

### 3. Ingestion of Food in Contact with VDC-Containing Polymer Food Wrap

VDC copolymers can be used in food wrap applications. Dow estimated the potential ingestion exposure that could result if VDC monomer migrates from a food wrap to food that is then ingested. Conservative estimates were developed for children and adults.

Standard FDA methods and assumptions were used to estimate the daily intake of VDC ingestion. The amount of VDC that migrates from PVDC food wrap was measured using peanut oil heated to 212 °F. The estimated daily was 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 residual VDC and the concentration of VDC in the food that results from the contact. The estimated daily intake of VDC was estimated to be less than 0.011 ug/kg/day for an adult and less than 0.0375 ug/kg/day for a child.

### 4. Inhalation of VDC in Residential Indoor Air from Carpet Backing Emissions

VDC-containing polymers are components in some latex emulsions that are used in carpet manufacturing. Residual VDC may migrate from the carpet into residential indoor environments and result in inhalation exposures to residents.

Dow used an indoor air modeling approach to estimate exposures. Two scenarios were used. In the first scenario it was assumed that carpet covered all the floors in the indoor space, that no VDC residual monomer is lost curing the latex during manufacturing or during storage prior to installation of the carpeting. An air exchange rate of 0.3 changes per hour was used. The space has a ceiling height of 8 feet. All of the residual monomer was assumed to be released

immediately and then the average concentration over a five year period was estimated. In the second scenario the residual monomer release rate was assumed to follow a first order decay with a release half-lives of 2 weeks, 1 year and 5 years. The average concentration over 5 years was estimated for each of the 3 emission decay half-lives. Three different half-life scenarios were used because the actual half-life is not known. All other assumptions in the second scenario are the same as the in the first scenario.

The estimated 5 year average indoor air concentrations ranged from 0.032 ug/m<sup>3</sup> to 0.0634 ug/m<sup>3</sup>. All the estimated 5 year average air concentration values were below the California chronic inhalation reference exposure level of 70 ug/m<sup>3</sup>.

## 5. Aggregate Exposure

Dow estimated the central tendency and high end aggregate exposures to children resulting from the four scenarios discussed above. The central tendency estimate was 0.065 ug/kg/day and the high end estimate was 0.15 ug/kg/day.

### 3.0. Summary of Tier 1 Hazard Assessment

#### Mutagenicity

The available data suggest that VDC produces genotoxic and cytotoxic effects in a number of test systems *in vitro*. In most cases, VDC causes bacterial mutations in multiple strains of Salmonella and E. coli and in the presence of an exogenous activation system. VDC induced chromosome aberrations and sister chromatid exchanges in cultured mammalian cells *in vitro* and DNA damage in mice treated *in vivo*.

#### Acute Toxicity

Numerous acute lethality studies on VDC have been conducted via the oral and inhalation routes in rats, mice, and hamsters. Mice appear to be more sensitive than either rats or hamsters to the acute toxicity from VDC. Oral LD<sub>50s</sub> ranged from 800-2000 mg/kg in rats to between 170-235 mg/kg in mice. The 4-hour LC<sub>50</sub> ranged from 1600 mg/m<sup>3</sup> for fasted rats to 60,000 mg/m<sup>3</sup> for non-fasted rats. The 4-hour LC<sub>50</sub> ranged from 140 mg/m<sup>3</sup> to 500 mg/m<sup>3</sup> in fasted mice. The 4-hour LC<sub>50</sub> ranged from 6600 mg/m<sup>3</sup> to 11,700 mg/m<sup>3</sup> for non-fasted hamsters and 600 mg/m<sup>3</sup> to 1800 mg/m<sup>3</sup> for fasted hamsters.

Numerous short-term, acute toxicity studies on VDC have also been conducted via the oral and inhalation routes in rats and mice. Acute exposures ranging from single exposures to up to 5 days showed various effects such as decreases in the serum levels of various liver enzymes, morphological changes in the liver, increased kidney weights and blood urea nitrogen and creatine levels, and histopathological changes in the kidney. These effects were observed

following oral exposures that ranged from 200-600 mg/kg and inhalation exposures  $\geq$  250 ppm.

### Repeated Dose Toxicity

VDC has been studied in repeat-dose studies in rats, mice, hamsters, rabbits, dogs and monkeys. Many of the studies, while providing qualitative toxicity information, are not adequate by current data quality standards to be used for quantitative assessment because they use too few animals, only one or two dose levels, lack controls, or have other major deficiencies. Qualitatively, in multiple species with exposures from 14 days to two-year duration, liver toxicity is the most common effect with kidney toxicity also noted often. Several studies report no effect at any dose tested or only report lethality. Selected studies which offered data that appears to be of the quality to use for quantitative assessment of toxicity are summarized.

An oral gavage study of male and female F344 rats tested doses of VDC administered in corn oil 5 days a week for 13 weeks. The NOAEL was 40 mg/kg (equivalent to 28.5 mg/kg-day). The LOAEL is 100 mg/kg (equivalent to 71.4 mg/kg-day) based on minimal to mild hepatocytomegaly. The inhalation toxicity of VDC was studied with black-hooded Wistar rats and 2 dosing regimes. The LOAEL was 50 ppm continuous exposure for 4 weeks (except two 1.5 hour periods per week). The rats showed liver injury including fatty changes in variable numbers of hepatocytes and only very occasional focal liver cell necrosis.

An oral gavage study of male and female B6C3F1 mice tested doses of VDC administered in corn oil, 5 days a week for 13 weeks. The NOAEL was 40 mg/kg (equivalent to 28.5 mg/kg-day). The LOAEL is 100 mg/kg (equivalent to 71.4 mg/kg-day) based on centrilobular necrosis of the liver.

A test of chronic oral VDC exposure in drinking water exposed male and female Sprague-Dawley rats for 2 years. The only treatment-related effect was minimal hepatocellular midzone fatty change and hepatocellular swelling. The changes were statistically significant only at the highest dose of 200 ppm. The NOAEL in male rats is 10 mg/kg-day and the LOAEL is 20 mg/kg-day based on the fatty liver effect. The NOAEL in female rats is 9 mg/kg-day and the LOAEL is 14 mg/kg-day for the same endpoint.

Chronic oral toxicity in male and female F344 rats was studied by gavage in corn oil for 104 weeks. The results suggested the maximum tolerated dose was not achieved. Histopathological examination indicated chronic renal inflammation in both male and female rats. However, this effect was only statistically significant in males at the highest test dose and because the effect is commonly detected in aged albino rats, it is not considered biologically significant. A chronic study of Sprague-Dawley rats exposed to VDC by gavage for 52 weeks and observed until spontaneous death (147 weeks) also detected no biologically significant effects at the study's end.

Several one year and longer inhalation toxicity studies of rats showed no statistically or biologically significant effects. One study exposed male and female Sprague-Dawley rats to VDC 6 hrs/day, 5 days/wk for up to 18 months. The surviving animals were held without treatment for an additional 6 months. In male and female rats minimal hepatocellular fatty change in the midzonal region of the hepatic lobule was observed at interim sacrifices after 6 months of exposure in groups exposed to 25 and 75 ppm. The fatty change was also observed in the 12 month sacrifice but there was no indication of progression in male rats. At the 18 month sacrifice (at the end of exposure) the effect was no longer observed in males but the effect persisted in females. At the end of the study, 6 months after exposure had ceased, the effect was no longer discernible.

The NOAEL for female rats was 25 ppm and the LOAEL was 75 ppm based on the fatty change in liver, considered a minimal, although reversible, adverse effect. The NOAEL for male rats was the highest dose tested, 75 ppm.

A chronic toxicity and carcinogenicity study of mice exposed to VDC by gavage in corn oil noted increased necrosis of the liver at 2 and 10 mg/kg. However, the effect was not statistically significant at either exposure. Several 12 month or longer inhalation toxicity and/or carcinogenicity tests of VDC were performed using mice. None identified biologically or statistically significant noncancer effects.

### Cancer

The carcinogenicity of VDC has been evaluated in rodents (primarily mice) following inhalation, oral, dermal and subcutaneous exposure. Of these carcinogenicity studies, one inhalation study in mice provides evidence of a positive carcinogenic effect of increases in renal adenocarcinomas in males. Mammary gland carcinomas and lung tumors (most of which were benign) were also observed. Other studies although negative, noted increases in a variety of malignant and benign tumors. These increases were either not statistically significant or judged not exposure-related by the study authors. Study limitations that reduce the sensitivity of these bioassays include less than lifetime exposure, doses below the maximum tolerated dose, small numbers of animals, and limited gross and microscopic tissue examinations.

Under draft revised guidelines for carcinogen risk assessment, EPA concluded VDC exhibits *suggestive evidence* of carcinogenicity but not sufficient evidence to assess human carcinogenic potential following inhalation exposure based on rodent studies. The finding that male mice developed kidney tumors in a lifetime bioassay is tempered by the absence of similar results in female mice or rats of either sex. Furthermore there are enzymatic differences (CYP2E1) between male mice and female mice, rat, and human kidney cells that may contribute to the sensitivity of male mice. EPA concludes the data are inadequate to assess human carcinogenic potential by the oral route based on the absence of statistically or biologically significant tumor increases in limited rodent bioassays by oral exposure. Human epidemiological

results are too limited to draw useful conclusions.

### Reproductive Toxicity

Reproductive and developmental toxicity of VDC was evaluated in an oral multi-generation reproductive toxicity study in rats. Three generations of male and female Sprague-Dawley rats were exposed to doses as high as 200 ppm via drinking water ad libitum during mating, gestation, and lactation. Histopathologic examination of the adult animals revealed mild pathologic changes in the liver at  $\geq 100$  ppm which were considered to be reversible in nature. There were no treatment-related effects observed on body weight, food or water consumption, selected organ weights (brain, heart, liver, kidneys, and testes), selected organ histopathology (liver, kidney, or any organs with visible signs of gross morphology); or on fertility, reproductive, or gestational parameters (that included mating day, parturition day, number live/dead pups newborn and number during lactation, litter weights, pup body weights, pup sex, number of rats pregnant/number mated, live pups/litter size, and pup survival indices). Pups were weighed and sexed and examined for external anomalies and any signs of toxicity. Liver and kidneys were weighed and examined microscopically. Observations on pups were unremarkable. The NOAEL for adult and reproductive/developmental toxicity from this study was considered to be 200 ppm (~30 mg/kg/day) VDC, the highest dose tested.

### Developmental Toxicity

Numerous prenatal developmental toxicity studies on VDC have been conducted via the oral and inhalation routes in rats, mice, and rabbits. Prenatal developmental toxicity studies in pregnant rats, mice, and rabbits exposed to VDC via inhalation during gestation resulted in increased incidence of skeletal variations, delayed ossification, and hydrocephalus in rat pups; and skeletal variations and delayed ossification in mice and rabbits; and reduced body weight (and in some cases, maternal mortality) in dams exposed to concentrations between 60 and 640 mg/m<sup>3</sup>. Oral exposure during gestation in rats produced no evidence of either maternal or developmental toxicity to doses as high as 200 mg/l in drinking water.

One laboratory had shown developmental variations in the heart following direct infusion of VDC into the uterus of pregnant rats or ingestion of VDC by pregnant rats from drinking water. There are significant issues in the interpretation of this study. The results of five other developmental toxicity studies did not show the cardiac effects. The IRIS external peer review panel identified significant problems with the reporting of the methods and dosing in that study and recommended that this study not be used to derive the RfD. The same issues were raised by the VCCEP peer consultation panel.

Although no specific developmental neurotoxicity studies have been conducted with VDC, an inhalation prenatal developmental toxicity study in rats exposed to concentrations as high as 283 ppm conducted a battery of behavioral tasks in pups tested at various times from

PND 1-21 (including surface righting, pivoting, auditory startle, bar holding, righting in air, visual placing, swimming ability, physical maturation, and activity). No adverse effects were observed on any of these parameters.

#### 4.0 Summary of Tier 1 Risk Characterization

In June, 2002, EPA finalized an IRIS assessment of VDC. The RfD was based on liver toxicity in a 2-year rat drinking water study, and was calculated from the BMDL<sub>10</sub> of 4.6 mg/kg/day and a composite uncertainty factor of 100; the resulting RfD is 0.05 mg/kg/day. The RfC was also based on liver toxicity in a 18-month rat inhalation study, and was calculated from the BMCL<sub>HEC</sub> of 6.9 mg/m<sup>3</sup> and a composite uncertainty factor of 30; the resulting RfC is 0.2 mg/m<sup>3</sup>. The sponsor used these RfD and RfC values for the risk characterization.

The sponsor characterized risk to children ages 1 - 18 years for single exposure pathways and aggregate exposures. For single pathways, the estimated oral exposures were compared to the RfD and the estimated inhalation exposures were compared to the RfC. In all cases, the estimated exposures were below the respective RfD and RfC. For aggregate exposures, it was necessary to combine the exposures from all pathways. The following rationale was applied. VDC is well absorbed by the inhalation route, and there is no portal of entry effect at chronic doses; in fact, the liver is the target following oral and inhalation exposure. Therefore, the estimated inhalation exposures were converted to equivalent oral exposures by assuming 100% absorption and applying the appropriate breathing rate for children. The converted inhalation values were then combined with the estimated oral exposures to derive the estimated aggregate exposure. The risks to children of ages 1 - 18 years were then estimated by two methods. A Margin of Safety (MOS) was calculated as the RfD divided by the exposure, and a Margin of Exposure (MOE) was calculated as the BMDL<sub>10</sub> divided by the exposure. Each of these was calculated for central tendency and high end exposures. The results are summarized in Table 1.

Table 1. Summary of Sponsor's MOS and MOE Calculations for VDC

Exposure Scenario	Central Tendency Estimates			High End Estimates		
	Exposure $\mu\text{g}/\text{kg}/\text{day}$	MOS	MOE	Exposure $\mu\text{g}/\text{kg}/\text{day}$	MOS	MOE
Ambient air	0.024 <sup>a</sup>	2100	190,000	0.072 <sup>b</sup>	690	64,000
Indoor air - carpet	0.023 <sup>c</sup>	2200	200,000	0.027 <sup>d</sup>	1900	170,000

Drinking water	0.008 <sup>c</sup>	6250	575,000	0.014 <sup>f</sup>	3600	330,000
Oral - food wrap	0.010 <sup>g</sup>	5000	460,000	0.0375 <sup>h</sup>	1300	120,000
Total exposure	0.065	770	77,000	0.15	330	31,000

a- 20% of the median value overestimate for children aged 1 to 18 years

b- 20% of the 95th %-tile overestimate for children aged 1 to 18 years

c- 80% of the value obtained using the maximum air concentration of 0.063 µg/m<sup>3</sup> and the mean inhalation rate of children aged 1 to 12 years of 0.441 m<sup>3</sup>/kg/day

d- 80% of the value obtained using the maximum air concentration of 0.063 µg/m<sup>3</sup> (Fontaine 2002b) and the 90th %-tile inhalation rate of children aged 1 to 12 years of 0.5405 m<sup>3</sup>/kg/day

e- The median overestimate for children aged 1 to 12 years

f- The 95th %-tile overestimate for children aged 1 to 12 years

g- Estimated using 1 kg of food only ingestion per day per child

h- Estimated using 3 kg of food and drink ingestion per day per child

## 5.0 Summary of the Sponsor's Tier 2 Data Needs

With respect to exposure, the sponsor noted that the potential for exposure has been well characterized. The assessment provided a review of the VDC life cycle and customer surveys as well as assessments of ambient air, drinking water and four end-use applications relevant for children of ages 1 - 18 years. The sponsor concludes that there is extremely limited potential for consumer exposure because only low levels of VDC remain in the polymers. The assessment also states that one of the greatest potential environmental sources of VDC is the degradation of 1,1,1 - trichloroethane but notes that production of this chemical was phased out under the Montreal Protocol.

The sponsor noted that the toxicity database that is available for VDC is quite extensive. Studies are available to adequately address the endpoints in tier 1, and in addition, many of the studies in tiers 2 and 3 have already been conducted. The only tier 2 study that has not yet been conducted is the immunotoxicity study, and tier 3 studies that have not been conducted are the neurotoxicity screening battery and the developmental neurotoxicity study. The sponsor, however, states that many of the endpoints that are included in these studies have been assessed in the context of the repeat dose studies or the developmental and reproductive toxicity studies; the lack of effects suggests that more detailed analyses are not warranted.

Finally, the sponsor states that the large MOS and MOE values that were calculated in the risk characterization section suggests that the typical childhood aggregate exposure to VDC is reasonably expected to be inconsequential. Given this, the sponsor concludes that no further

exposure or hazard studies are warranted given present and future use conditions.

## 6.0 EPA Response to the Sponsor's Tier 2 Data Needs

EPA agrees with the approach of using quantitative estimates of risk to help inform decisions about the potential impact of additional exposure or toxicity studies, and therefore assist in determining whether "data gaps" are actually "data needs". As discussed above, the sponsor used a MOS and MOE approach to quantify risks to children. For the MOS calculations, a recent RfD was used, and the BMDL<sub>10</sub> from the study used for the derivation of the RfD was used for the MOE calculations. Both approaches yielded values that are quite large. EPA agrees that these are useful approaches, and that they may actually be very conservative for assessing potential risks to children (or prospective parents) from exposure to VDC.

By definition, the RfD is derived to provide protection for lifetime, chronic exposures. While the chronic RfD is protective of children, it does not specifically address toxicities for less than lifetime exposures which would be typical of a child. Recently, EPA has published a report by the RfD/RfC Technical Panel that recommends the derivation of several less than lifetime reference values which may be more appropriate for specifically addressing the potential risks to children (or to prospective parents). In many cases, the less than lifetime reference values will be higher than the chronic RfD or RfC. Thus, use of the chronic RfD or RfC (or BMDL<sub>10</sub> from the "critical" study) for the MOS and MOE calculations may often be quite conservative. For VDC, the chronic RfD is based on liver toxicity in a 2-year bioassay in adult rats. In the multigeneration reproductive toxicity study, which was conducted at similar dose levels as the 2-year bioassay, there was no evidence of liver toxicity in weanlings (21 days) that had been exposed to VDC prenatally and during lactation. Therefore, EPA is confident that the use of the chronic RfD (or BMDL<sub>10</sub>) in the sponsor's calculations is quite conservative.

EPA agrees that the exposure assessment is quite extensive, but notes that there are some transparency issues in the original assessment. Six of the ten plausible scenarios were excluded because exposures were not expected to occur or to be negligible. However, no data were presented to support this. This issue was clarified in a letter from the Dow Chemical Company dated May 23, 2005, which provided the rationale for excluding those scenarios.

EPA also notes that it is not clear whether conservative assumptions were made for the carpet exposure scenario. The carpet scenarios present 5 year average air concentrations in indoor environments. Since emission rates are probably not constant over time but start out high and then decrease, estimates of how the indoor air concentrations change over time for each of the different scenarios would be informative rather than just providing 5 year average concentrations. This would improve the transparency of the assessment if it could be demonstrated that the initial high exposures were inconsequential. To address this issue, the Dow Chemical Company provided an eight page study entitled "Examination of Short Term "Spike" Indoor Air Concentration Assuming Instantaneous Release of Vinylidene

Chloride(VDC) From VDC Based Latex in Carpet" dated January 19, 2005. This study provided additional scenarios for indoor air exposures using conservative assumptions such as; the USEPA recommended air exchange rates, no VDC monomer is lost from the wet latex during the manufacturing and transport and that 100% of the VDC is lost instantaneously upon installation. The study concludes that in order to exceed EPA's RfC of  $200 \mu\text{g}/\text{m}^3$  one would need to replace the carpet every 13.5 hours and to exceed California's guidance level of  $70 \mu\text{g}/\text{m}^3$  one would need to replace the carpet more frequently than every other day. EPA acknowledges these assumptions to be sufficiently conservative for residential scenarios. The study also acknowledges that the same approach can be used to estimate exposures to workers.

EPA notes that two other tier 1 exposure scenarios were not included in the assessment. One of these involves VDC inhalation exposures resulting from intrusion of VDC vapors from a contaminated groundwater source into residences. This scenario was discussed at the peer consultation meeting and was identified as one of the scenarios that could lead to the highest exposures. On January 19, 2005, the Dow Chemical Company provided a two page summary of the indoor air concentrations of VDC obtained from the Redfield site in Denver Colorado. The data provided showed that pre-mitigation indoor air concentrations listed for the Redfield site did not exceed the  $200 \mu\text{g}/\text{m}^3$  IRIS RfC, although 14 of the 691 concentrations exceeded the California chronic inhalation REL of  $70 \mu\text{g}/\text{m}^3$ . It went on to state that all mitigated residences had measured indoor air concentration less than  $0.49 \mu\text{g}/\text{m}^3$ . EPA notes that this supplies the needed information previously missing on this issue for Tier 1 assessment.

The second scenario involves providing conservative model estimates of ambient air concentrations (e.g. fence line concentrations) and potential inhalation exposures resulting from releases at industrial facilities. Fence line ambient air concentrations and exposure estimates may be higher than the estimates provided in the assessment.

Finally, EPA notes that the sponsor excluded consideration of exposures to prospective parents through occupational or other exposures. The rationale that was provided was that there were no indications of reproductive effects following exposure to VDC. EPA notes, however, that there is some evidence of potential developmental effects following prenatal exposures in animal studies, and therefore notes this should be included in a tier 1 assessment. This issue was clarified in a letter dated March 7, 2005, in which the Dow Chemical Company provided a study entitled "Vinylidene Chloride: Developmental Toxicity Study Findings in Relation to Occupational Exposure." The study stated 'measurements in production facilities are reported to be much lower than 5 ppm and this was reconfirmed during industrial hygiene monitoring in 2001 and 2002. The study does not include specifics on the industrial hygiene monitoring and the workplace where the monitoring was conducted.

In conclusion, EPA agrees that with the additional information that was provided in the letters submitted on January 19, 2005, March 7, 2005, and May 23, 2005 the Tier 1 exposure assessment is complete. EPA does not recommend any Tier 2 exposure analyses of VDC for

## VCCEP:

EPA agrees that the existing toxicology database is quite extensive and adequately covers the studies in tier 1, and also includes some of the studies in tiers 2 and 3. There are several deficiencies in the existing multi-generation reproductive toxicity study that introduce some uncertainties in assessing risks to children and prospective parents including a lack of organ weight or histopathology data on female reproductive organs or histopathology on testes; no measurements of estrous cyclicity; nor any observations on sperm number, morphology or motility. EPA recognizes that this particular study was conducted in conjunction with a 90-day and 2-year bioassay which did include a histopathological evaluation of these organs; however, some uncertainties still exist as no evaluation has been conducted on the F1 animals which represent a unique population in that they have been exposed throughout pre- and postnatal development.

EPA also notes that there is some controversy regarding the interpretation of the results of the Dawson (1993) prenatal developmental toxicity study which noted heart abnormalities. The IRIS external peer review panel identified significant problems with the reporting of the methods and dosing in this study. The study authors were contacted directly in order to obtain enough information to estimate the actual exposure of the animals. The IRIS panel concluded that there are substantial problems with the study, and that it should not be used to derive the RfD. This study was also discussed by the peer consultation panel. The majority of the peer consultation panel thought that, although the study does raise questions, the results are clearly inconsistent with five other developmental toxicity studies. Some panelists recommended that the results of the study be clarified by redoing the statistics, re-examining the tissues, and interviewing the investigators regarding methodology. Other panelists did not think any additional work was needed. EPA also notes that in the multi-generation reproductive toxicity study, a full necropsy was conducted at weaning on all F1 pups that were not to be continued on study as part of the F1 parental generation. No heart defects were noted in the pups, or at necropsy of the F1 parental generation, and survival of the F1 parents was not affected.

Specific toxicology data gaps that exist are the immunotoxicity study in tier 2, and the neurotoxicity screening battery and developmental neurotoxicity study in tier 3. Given the use of the chronic RfD and the magnitude of the MOE and MOS calculations for children, it is very unlikely that additional toxicity information would substantially impact these calculations. Therefore, EPA does not consider the toxicology "data gaps" to be actual "data needs" at this time.