
Review of Current Quantitative Cancer Risk Assessment
Evaluations By EPA, Review of the Air Dispersion Model
employed by the Vista Chemical Company Aberdeen,
Mississippi, and Estimation of Cancer Risks at Different
Distances from Emission Sources from the Vista
Chemical Company Facility

Prepared by:
Clement International Corporation
9300 Lee Highway
Fairfax, Virginia 22031

Prepare for:
Vista Chemical Company
P.O. Box 91
Aberdeen, Mississippi 39730

February 4, 1991

Introduction

This report reviews and compares the use of two inhalation unit risk values that are reported in two different EPA documents for vinyl chloride. Comments are made as to the scientific validity of the unit risks values for estimating acceptable ambient air concentrations to protect human health, and a review was conducted on the air dispersion model used by Vista Chemical Company in their Aberdeen, Mississippi plant to characterize emissions levels. Exposures estimated from the model were then used to determine human cancer risks at different points from the emission sources under different production conditions.

Review and Comparison of Determining Acceptable Ambient Air Concentrations for Vinyl Chloride Based on Carcinogenicity in two EPA Reports

There are two recent EPA documents in which estimates were derived for $q1^*$ values for vinyl chloride. In the first document (Health Effects Assessment for Vinyl Chloride, EPA, 1984, Office of Health and Environmental Assessment, EPA/540/1-86-036) the animal $q1^*$ was given as $4.23 \times 10^{-3} \text{ (mg/kg/day)}$ and the human $q1^*$ was given as $2.5 \times 10^{-2} \text{ (mg/kg/day)}^{-1}$ (see Appendix 1 for determination of animal $q1^*$ value using GLOBAL86). Inhalation studies in rats were used and total tumors were used as the toxicological endpoint. This $q1^*$ value can be converted to units of ppm^{-1} or $\text{(ug/m}^3\text{)}^{-1}$ as follows by employing the same conversion factors used by EPA in converting animal exposures in ppm to human equivalent exposures in mg/kg/day:

1. Correction for surface area between humans and rats

$$[(1/(70 \text{ kg human}/.35 \text{ kg rat}))^{1/3}] * 2.5 \times 10^{-2} = 4.27 \times 10^{-3} \text{ (mg/kg/day)}^{-1}$$

2. Adjustment for body weight of rat

$$4.27 \times 10^{-3} / .35 \text{ kg rat} = 1.22 \times 10^{-2} \text{ (mg/day)}^{-1}$$

3. Adjustment for breathing rates of rats

$$.223 \text{ m}^3/\text{d} * 1.22 \times 10^{-2} = 2.72 \times 10^{-3} \text{ (mg/m}^3\text{)}^{-1} \text{ or}$$

$$2.72 \times 10^{-6} \text{ (ug/m}^3\text{)}^{-1} \text{ or}$$

$$2.56 \times 10^3 \text{ (ug/m}^3\text{*ppm)} * 2.72 \times 10^{-6} \text{ (ug/m}^3\text{)}^{-1} =$$

$$6.96 \times 10^{-3} \text{ ppm}^{-1} \text{ (EPA84 calculation was } 6.80 \times 10^{-3} \text{ ppm}^{-1}\text{)}$$

4. It was assumed that all the vinyl chloride inhaled was absorbed into systemic circulation. This is a conservative estimate.

5. The previous $q1^*$ value that the state of Mississippi used to determine cancer risk was $4.1 \times 10^{-6} \text{ (ug/m}^3\text{)}^{-1}$. This value is greater than the calculated value of $2.72 \times 10^{-6} \text{ (ug/m}^3\text{)}^{-1}$ in step 3 above by 1.5.

In a more recent update (Health and Environmental Effects Profile for Chloroethene, EPA, 1985, Environmental Criteria and Assessment Office ECAO-Cinn-P155) the rat $q1^*$ was determined to be $5.04 \times 10^{-2} \text{ (mg/kg/day)}$ (see Appendix 2 for determination of the rat $q1^*$ value using GLOBAL86) and the human $q1^*$ was determined to

be 2.95×10^{-1} (mg/kg/day) $^{-1}$. Animal studies from the same investigator were used as in the EPA 1984 report; instead of using total tumor incidence, however, angiosarcomas of the liver were used as the only toxicological end point. Corrections to the dose were made since the observation period was extended after exposure stopped and an assumption was made that only 50% of the inhaled vinyl chloride was being absorbed. By using the same conversion factors above and correcting for % uptake the following inhalation $q1^*$ was determined.

1. Correction for surface area between humans and rats

$$[(1/(70/.35))^{1/3}] * 2.95 \times 10^{-1} \text{ (mg/kg/d)}^{-1} = 5.05 \times 10^{-2} \text{ (mg/kg/d)}^{-1}$$

2. Adjustment for body weight and breathing rate of rats

$$[5.05 \times 10^{-2} \text{ (mg/kg/d)}^{-1} / .35 \text{ kg}] * .223 \text{ m}^3/\text{d} = 3.22 \times 10^{-2} \text{ (mg/m}^3\text{)}^{-1}$$

$$\text{or } 3.22 \times 10^{-5} \text{ (ug/m}^3\text{)}^{-1}$$

3. In this assessment EPA assumed that only 50% of the vinyl chloride was absorbed through the lungs. To correct for this the $q1^*$ value has to be multiplied by .5.

$$(.5) * 3.22 \times 10^{-5} \text{ (ug/m}^3\text{)}^{-1} = 1.61 \times 10^{-5} \text{ (ug/m}^3\text{)}^{-1}$$

$$\text{or } 4.12 \times 10^{-2} \text{ ppm}^{-1}$$

The state of Mississippi is recommending a $q1^*$ value of 4.2×10^{-5} (ug/m³) $^{-1}$. This value is derived from the more recent EPA report just described from the $q1^*$ value of 2.95×10^{-1} (mg/kg/d) $^{-1}$. This number is 2.6-fold greater than the number calculated above (1.61×10^{-5}). Mississippi derived their number as follows.

$$[2.95 \times 10^{-1} \text{ (mg/kg/d)}^{-1}] * (.5) * (20 \text{ m}^3/\text{d}) * (10^{-3} \text{ mg/ug}) / 70 \text{ kg} = 4.21 \times 10^{-5} \text{ (ug/m}^3\text{)}^{-1}$$

This calculation is incorrect, since the same conversion factors used by EPA to convert experimental levels (ppm) to human exposure equivalents (mg/kg/day) were not used by the state of Mississippi to back-calculate from (mg/kg/day) to ppm or ug/m³.

Analysis of the data used by EPA in determining a human $q1^*$ of 2.95×10^{-1} (mg/kg/day) $^{-1}$ in their 1985 report

Figure 1 illustrates the relationship between liver angiosarcoma and vinyl chloride exposure in rats. No dose-response relationship is obvious. Furthermore, EPA did not use all the data in determining the $q1^*$ value. It only selected data points 0, .172, .344 and .86 mg/kg/day. There was no rationale provided why other data points were omitted. In addition, the data points are not even taken from the same experiment. For example, data

points 0.344 and 0.86 were from Maltoni et al. experiment BT15 and data point 1.719 was taken from Maltoni et al. experiment BT1. Therefore, the manner in which the $q1^*$ value was calculated is scientifically incorrect and meaningless.

In the 1985 report the length of the experiment was reported to be up to 1029 days, whereas the exposure period to vinyl chloride was for 365 days. In the transformation of experimental doses to human equivalent doses an adjustment factor of 365/1029 was used. From a biological sense this dose-averaging approach may not be appropriate. The actual time to tumor data needs to be obtained in order to make the appropriate adjustments to dose.

The first $q1^*$ value established by EPA in 1984 was based on total tumors rather than liver angiosarcomas. Although in some instances total tumors may not provide the most sensitive assessment of cancer risk, the data as shown in figure 2 do show a linear dose response relationship up to 239.1 mg/kg/day. Therefore, these data provide a much better data base to determine a human $q1^*$ value, than the data base given in the EPA 1985 report.

Discussions with EPA's Human Health Assessment Group

EPA's Office of Health and Environmental Assessment often has contractors provide health profiles and reports on various chemicals. These documents are used primarily as guidance to provide available information on the toxicity of various environmental agents and to provide the agency scientists and regulators with initial data to determine what chemicals potentially should take greater priority in being regulated. Although these documents have undergone some peer review within EPA they have not undergone the extensive scientific peer review that is usually necessary to support program office regulations. The more recent 1985 EPA report entitled "Health and Environmental Effects Profile for Chloroethene," which is being used by the State of Mississippi, is a first draft report and has the disclaimer that it is "for review purposes only and does not constitute Agency policy." Discussions with EPA scientists in the Human Health Assessment Group revealed that they are aware of the deficiencies in the approach taken in the 1985 EPA report for calculating a $q1^*$ value for vinyl chloride and that additional evaluations of the data base are necessary to derive a more scientifically sound quantitative risk assessment.

Discussion

The state of Mississippi elected to use a unit risk factor of $2.95 \times 10^{-1} \text{ (mg/kg/day)}^{-1}$ taken from an EPA report "Health and Environmental Effects Profile for Chloroethene" September 1985. From this value they converted the units to obtain a $q1^*$ value of $4.21 \times 10^{-5} \text{ ug/m}^3$. This value is not appropriate to use to set

acceptable ambient exposure levels to vinyl chloride for the following reasons:

1. The conversion from mg/kg/day to ug/m³ was done incorrectly (see above). The correct conversion would reduce the unit risk by a factor of 2.6.
2. The calculation was performed using a q1* value that EPA has not endorsed. This is stated in the disclaimer in the 1985 document.
3. The data used in calculating the q1* value in the 1985 EPA report are not of sufficient quality to determine a q1* value.
 - a. There is no dose-response relationship.
 - b. Results from different experiments were pooled in order to get a dose response relationship without any scientific rationale provided.
 - c. Only certain data points were selected for determining the unit risk without any scientific rationale provided.
 - d. Two of the data points available in the original Maltoni et al. paper were not included in the 1985 EPA report. No scientific rationale was provided.
4. Vinyl chloride is known to require metabolic activation to the proximate carcinogen. These pharmacokinetic considerations were not incorporated into the dose-response data used in determining the unit risk determination in the 1985 EPA report.
5. Many other studies are available than Maltoni et al. to estimate the carcinogenic risk of vinyl chloride. These other studies should be assessed, and pharmacokinetic/biologically based models should be considered to estimate more accurately the human carcinogenic risk of exposure to vinyl chloride gas.

Conclusions

The use of the unit risk presented in the 1985 EPA report entitled "Health and Environmental Effects Profile for Chloroethene" to establish acceptable ambient levels of vinyl chloride in the air is not scientifically justifiable because of the misuse of the data, lack of critical peer review of the methods employed in the report, and insufficient use of critical data pertinent in considering the carcinogenic risk of vinyl chloride.

Until a more scientifically sound risk assessment is performed the former $q1^*$ value of $2.72 \times 10^{-6} \text{ (ug/m}^3\text{)}^{-1}$ from the 1984 EPA report entitled "Health Effects Assessment for Vinyl Chloride" should be used to estimate cancer risk for vinyl chloride in the air. Although there are also deficiencies in the data on which this $q1^*$ value is based, a solid dose-response relationship for total tumors (figure 2) was used to estimate risk.

APPENDIX 1

R

GLOBAL 86 (MAY 1986)

BY RICHARD B. HOWE AND CYNTHIA VAN LANDINGHAM

CLEMENT ASSOCIATES, INC
 1201 GAINES STREET
 RUSTON, LA 71270
 (318) 255-4800

vinyl chloride: data taken from EPA 1984 report
 (total tumors)

POLYNOMIAL DEGREE SELECTED BY PROGRAM, (POLY-DEGREE=0)
 CHI-SQUARE TEST USED IN SELECTION

GROUP	DOSE	#RESPONSES OBSERVED/#ANIMALS	#RESPONSES PREDICTED
1	.000000	6/ 58	9.81
2	4.90000	10/ 59	10.69
3	23.9000	16/ 59	13.35
4	47.8000	22/ 59	16.50
5	239.100	32/ 59	34.98

CHI-SQUARE GOODNESS OF FIT STATISTIC IS 5.6876

P-VALUE FOR THE CHI-SQ TEST WITH 3 DEGREES
 OF FREEDOM IS .1278379359

FORM OF PROBABILITY FUNCTION:

$P(\text{DOSE}) = 1 - \exp(-Q_0 - Q_1 * D - Q_2 * D^2)$

MAXIMUM LIKELIHOOD ESTIMATES OF DOSE COEFFICIENTS

Q(0) = .185324445807
 Q(1) = 2.983355597998E-03
 Q(2) = .000000000000

MAXIMUM VALUE OF THE LOG-LIKELIHOOD IS -163.144925015

CALCULATIONS ARE BASED UPON EXTRA RISK

GLOBAL 86 UPPER CONFIDENCE LIMITS ON RISK FOR FIXED DOSE

DOSE ----	MLE RISK -----	UPPER BOUND ON RISK -----	CONFIDENCE LIMIT SIZE -----	COEFFICIENTS FOR CONFIDENCE LIMIT -----
1.0000	2.97891E-03	4.22255E-03	95.0%	Q(0) = .15535 Q(1) = 4.23149E-03 Q(2) = .00000

NORMAL COMPLETION!

APPENDIX 2

GLOBAL 86 (MAY 1986)

BY RICHARD B. HOWE AND CYNTHIA VAN LANDINGHAM

CLEMENT ASSOCIATES, INC
 1201 GAINES STREET
 RUSTON, LA 71270
 (318) 255-4800

vinyl chloride: data taken from EPA 1985 report
 (liver angiosarcomas)

POLYNOMIAL DEGREE SELECTED BY PROGRAM, (POLY-DEGREE=0)
 CHI-SQUARE TEST USED IN SELECTION

GROUP	DOSE	#RESPONSES OBSERVED/#ANIMALS	#RESPONSES PREDICTED
1	.000000	0/363	.00
2	.344000	1/119	1.17
3	.860000	5/120	2.92
4	1.71900	1/ 60	2.89

CHI-SQUARE GOODNESS OF FIT STATISTIC IS 2.8312

P-VALUE FOR THE CHI-SQ TEST WITH 2 DEGREES
 OF FREEDOM IS .2427793524

FORM OF PROBABILITY FUNCTION:

$P(\text{DOSE}) = 1 - \exp(-Q_0 - Q_1 * D - Q_2 * D^2)$

MAXIMUM LIKELIHOOD ESTIMATES OF DOSE COEFFICIENTS

 $Q(0) = .000000000000$
 $Q(1) = 2.867931930907E-02$
 $Q(2) = .000000000000$

MAXIMUM VALUE OF THE LOG-LIKELIHOOD IS -33.1407703774

CALCULATIONS ARE BASED UPON EXTRA RISK

GLOBAL 86 UPPER CONFIDENCE LIMITS ON RISK FOR FIXED DOSE

DOSE	MLE RISK	UPPER BOUND ON RISK	CONFIDENCE LIMIT SIZE	COEFFICIENTS FOR CONFIDENCE LIMIT
----	-----	-----	-----	-----
1.0000	2.82720E-02	4.91334E-02	95.0%	$Q(0) = .00000$ $Q(1) = 5.03816E-02$ $Q(2) = .00000$

NORMAL COMPLETION!

Figure 1

EPA85 (liver angiosarcomas)

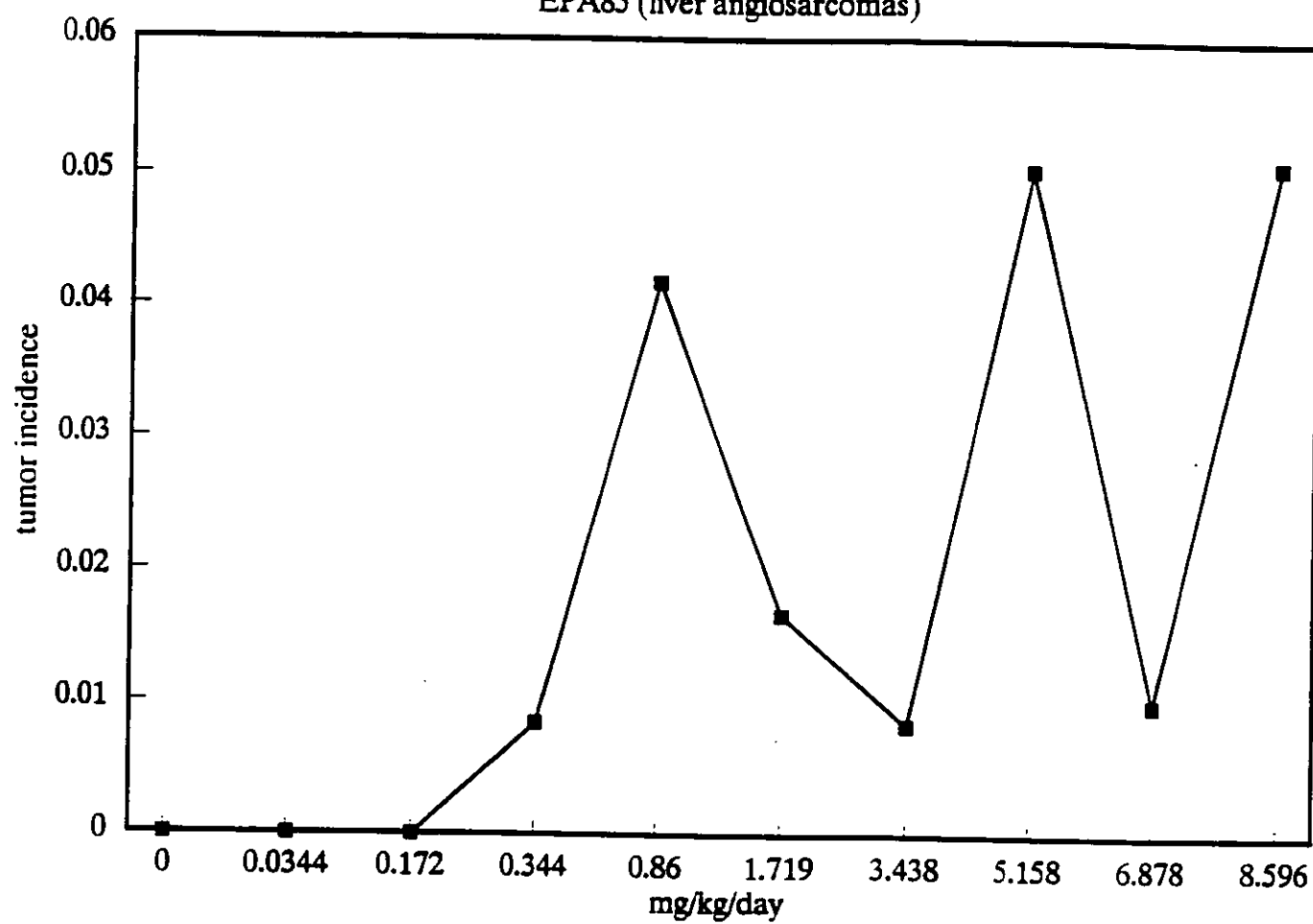
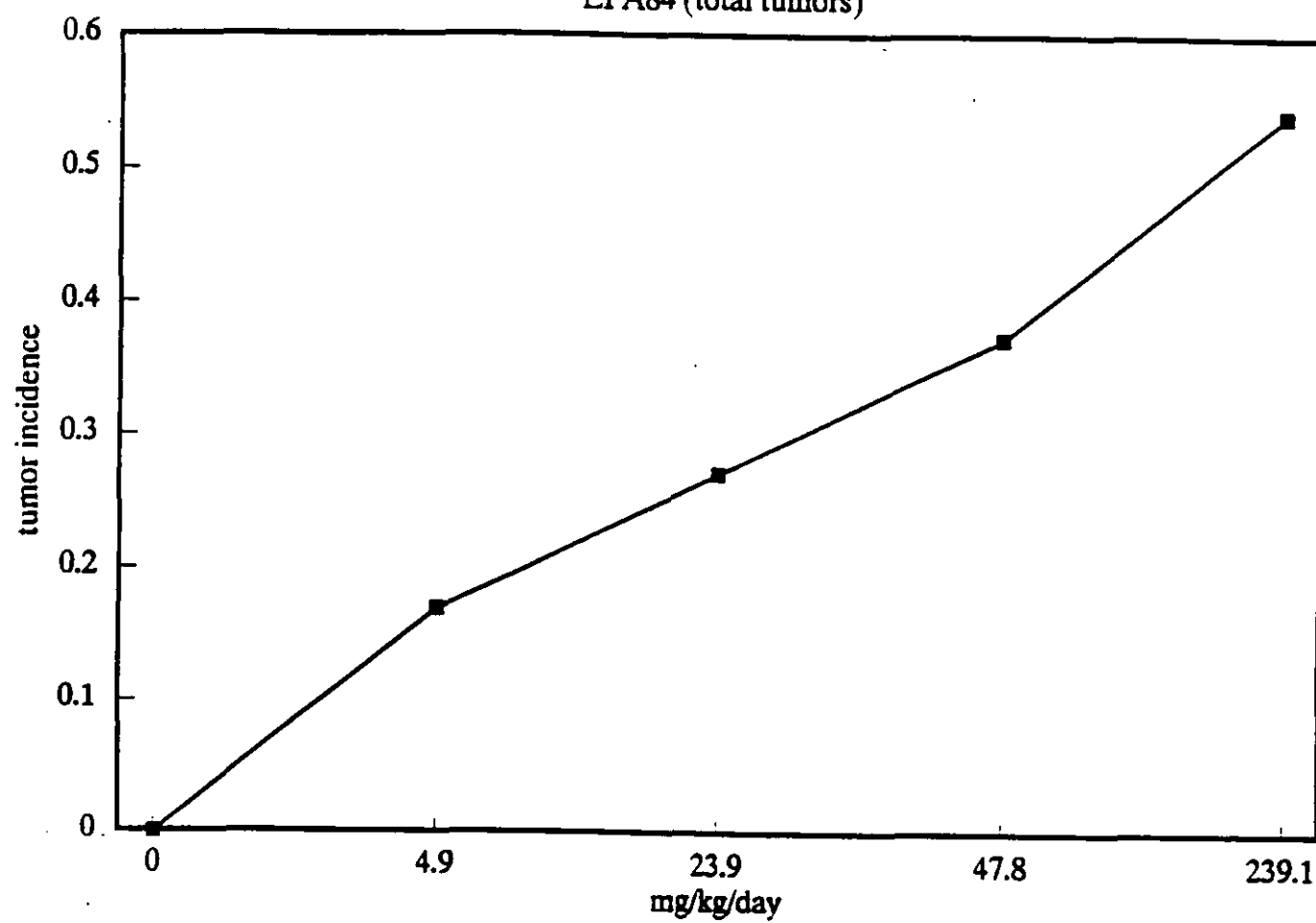


Figure 2

EPA84 (total tumors)



Inhalation Risk Assessment

An inhalation risk assessment was conducted for off-site exposures to vinyl chloride emissions from the Vista Chemical Company in Aberdeen, Mississippi. The potential inhalation risks were calculated by combining a unit risk factor for vinyl chloride with dispersion modeling results of emissions from the Vista Chemical Company plant. The dispersion modeling was conducted by personnel at the Vista Chemical Company plant and results were provided to Clement International, Inc. for use in the risk assessment.

Ambient air concentrations associated with vinyl chloride emissions were determined using the Industrial Source Complex Short-Term (ISCST) air dispersion model. ISCST is an EPA recommended model for use in industrial settings such as the Vista Chemical Company plant. The ISCST model was run in the regulatory default mode which automatically selects model options recommended for use by the EPA. Meteorological data from the Montgomery Alabama National Weather Service station, for the years 1966 to 1970 were used in the ISCST model. A separate model run was conducted for each of the five years of meteorological data using a polar grid with 36 radials (10 degrees of arc per radial) and receptors placed at 100, 150, 200, 300, 400, 500, 750 and 1000 meters from the plant along each radial.

Emissions from the plant were characterized in the ISCST model by 34 separate emission sources. These sources included both controlled stack emissions modeled as point sources, and fugitive emissions modeled as both volume and area sources. Analysis of the ISCST model results for each of the five years of meteorological data indicated that the 1970 data resulted in the highest annual average concentration for off-site receptors. A second ISCST model run was then conducted using the same emissions inputs and model options with a cartesian grid of receptor points at 200, 400, 600, 800, 1000, 1250, 1500, 1750, 2000, 3000, 3500, 4000, and 5000 meters from the plant in all directions. This resulted in model predictions of annual average concentrations at 676 receptors around the plant. The results from this model run were used by Clement International, Inc. in the inhalation risk assessment.

The first step in the inhalation risk assessment was to identify the receptor locations to be evaluated. Two receptor grids were constructed for evaluation. In the first receptor grid model receptors located within the fence line boundaries of the plant were eliminated from the evaluation. In addition, model concentrations for receptors beyond 3500 meters from the plant were also eliminated from the evaluation because the concentrations would result in negligible inhalation risks

relative to the closer receptor locations evaluated and in the majority of cases they were beyond the populated areas around the plant. The second grid used in the inhalation risk assessment used the same receptor locations as the first with the exception that receptors located within the plant boundaries but outside of the fence line were excluded.

For both of the grids evaluated in the inhalation risk assessment the maximum and average model predicted annual average concentrations were used. The average concentration used in the evaluation was the arithmetic average of all model predicted annual average concentrations for the receptors within each grid evaluated. Note that the use of an arithmetic average assumes an equal weighting of all model predicted concentrations. However, the spacing of the receptor grid increased with distance from the plant, while model predicted concentrations decreased with distance from the plant. Thus the average concentration used in this assessment is conservative since a regular spacing of the grid out to 3500 meters from the site would have included many more concentrations with lower values than those predicted for receptors located within 1000 meters of the plant, resulting in a lower arithmetic average concentration.

The ISCST model results used in the inhalation risk assessment were based on a 200 parts per million (ppm) vinyl chloride content in the slurry. The risk assessment however was conducted for a 150 ppm and 400 ppm vinyl chloride slurry concentration. According to Vista Chemical Company personnel the model results could be scaled for the changes in vinyl chloride slurry content. Vista Chemical Company personnel indicated that emissions from only a portion of the 34 sources evaluated in the ISCST model would be affected by changes in the slurry content. They had configured the ISCST model to calculate receptor concentrations separately for two source groups. One source group represented emissions from the 19 sources (source numbers 1-19) that were affected by slurry content. The second source group represented the 15 remaining sources (source numbers 20-34) whose emissions were unaffected by slurry content. The concentration at a receptor for all modeled vinyl chloride emissions from the plant is then the sum of the concentration at the receptor for each source group. Vista Chemical Company personnel provided the following algorithm to convert the 200 ppm slurry results to the desired slurry content:

$$x_t(x, y) = x_1(x, y) + x_2(x, y) * \frac{DSC}{200}$$

where:

x_t = concentration at a point due to all sources combined, (ug/m³),

x_1 = concentration at a point due to source numbers 20 to 34, (ug/m³),

X_2 = concentration at a point due to source numbers 1 to 19, (ug/m³),

DSC = the desired concentration of vinyl chloride in the slurry, (ppm).

Using the algorithm shown above for a 150 and 400 ppm concentration of vinyl chloride in the slurry with the ISCST model output and unit risk factor for vinyl chloride of 2.72×10^{-6} per ug/m³ yielded the following results:

- For a slurry concentration of 150 ppm vinyl chloride the average annual concentration for receptors located at or beyond the fence line was 0.66 ug/m³ for an inhalation risk of 2×10^{-6} ,
- For a slurry concentration of 150 ppm vinyl chloride the maximum annual concentration for receptors located at or beyond the fence line was 13.62 ug/m³ for an inhalation risk of 4×10^{-5} ,
- For a slurry concentration of 400 ppm vinyl chloride the average annual concentration for receptors located at or beyond the fence line was 1.65 ug/m³ for an inhalation risk of 4×10^{-6} ,
- For a slurry concentration of 400 ppm vinyl chloride the maximum annual concentration for receptors located at or beyond the fence line was 32.41 ug/m³ for an inhalation risk of 9×10^{-5} ,
- For a slurry concentration of 150 ppm vinyl chloride the average annual concentration for receptors located at or beyond the property line was 0.60 ug/m³ for an inhalation risk of 2×10^{-6} ,
- For a slurry concentration of 150 ppm vinyl chloride the maximum annual concentration for receptors located at or beyond the property line was 7.34 ug/m³ for an inhalation risk of 2×10^{-5} ,
- For a slurry concentration of 400 ppm vinyl chloride the average annual concentration for receptors located at or beyond the property line was 1.50 ug/m³ for an inhalation risk of 4×10^{-6} ,
- For a slurry concentration of 400 ppm vinyl chloride the maximum annual concentration for receptors located at or beyond the property line was 17.73 ug/m³ for an inhalation risk of 5×10^{-5} .

Model predictions for average and maximum air concentrations and the associated Cancer risks are summarized in Table 1.

Table 1

Model Predictions for Average/Maximum Annual Air
Concentrations of Vinyl Chloride and Associated Cancer Risks

Slurry Concentrations (ppm)	Average Concentration		Risk
	Fenceline (ug/m ³)	Property line (ug/m ³)	
150	0.66		2x10 ⁻⁶
150		0.60	2x10 ⁻⁶
400	1.65		4x10 ⁻⁶
400		1.50	4x10 ⁻⁶
Slurry Concentrations (ppm)	Maximum Concentration		Risk
	Fenceline (ug/m ³)	Property line (ug/m ³)	
150	13.62		4x10 ⁻⁵
150		7.34	2x10 ⁻⁵
400	32.41		9x10 ⁻⁵
400		17.73	5x10 ⁻⁵