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Subject: Risk Assessment of VCM Ingestion in Sprague-Dawley Rats

Summary

Data from two feeding studies by Maltoni with regard to the effect of VCM on Sprague-Dawley rats was combined to approximate the risk that might occur due to the presence of VCM in PVC film. A linear extrapolation model was employed to determine risk at very low doses. This was then applied to some hypothetical human diets in order to estimate the risk of cancer due to residual VCM in the film in which food is wrapped.

Discussion

Maltoni conducted two experiments (BT-11 and BT-27) in which male and female Sprague-Dawley rats were fed VCM in their daily diets, 4-5 days per week. In BT-11 the rats began this regimen at 13 weeks of age and continued for 52 weeks. Correspondingly, in BT-27, rats were started at 10 weeks of age and fed for 59 weeks on diets containing VCM. Both experiments were terminated at 136 weeks. Table 1 gives the combined data from BT-11 and BT-27 with respect to two responses, all malignant tumors and liver angiosarcomas.

Table 1

Combined Data for BT-11 and BT-27

Dose MG/KG	PPM*	Animals Tested	Malignant Tumors	Liver Angiosarcomas
0	0	230	35	0
0.03	0.6	150	27	0
0.3	6.0	150	20	1
1.0	20.0	150	38	3
3.33	66.6	80	8	0
16.65	333.3	80	24	10
50.0	1000 0	80	31	17

*In rats 1 MG/KG/Day = 20 PPM in diet.

This data was then fitted by a multi-stage model with low dose estimation being done by linear extrapolation.

In order to apply the results of this modeling to the risk of cancer in man certain assumptions had to be made concerning the total diet and the VCM in the film:

(1) The total diet consists of 1500 gm of food/day.
(2) It takes 1 sq. in. of film to wrap 10 gm of food.
(3) The film weighs 0.0159 gm per sq. in.
(4) All the residual VCM in the film migrates to the food.

It can be shown, from these assumptions that;

$$\text{VCM in Diet (PPM)} = (1.59 \times 10^{-3})\,vP \qquad (1)$$

Where,

v = VCM (PPM) in film
P = Proportion of diet wrapped in film

Notation: Let ΔR = increased risk,
and D = dose in PPM

Two responses were then considered:

(1) All malignant tumors
(2) Liver angiosarcomas

(1) All Malignant Tumors

From the data in Table 1,

$$\Delta R = (3.2494 \times 10^{-1})\ D = (5.1665 \times 10^{-4})\ v\ P \qquad (2)$$
$$D = (3.0775)\ R \qquad (3)$$

In Table 2 the increased risk of malignant tumors is compared for the multi-stage and linear extrapolation models.

Table 2

Increased Risk of Malignant Tumors

	Multi - Stage	95%		Linear Extrapolation
ΔR	D(PPM)	LCL	UCL	D
10^{-5}	3.59×10^{-2}	2.36×10^{-2}	5.46×10^{-2}	3.08×10^{-5}
10^{-6}	3.59×10^{-3}	2.36×10^{-3}	5.46×10^{-3}	3.08×10^{-6}
10^{-7}	3.59×10^{-4}	2.36×10^{-4}	5.46×10^{-4}	3.08×10^{-7}

In Table 3 the increased risk of malignant tumors is given as a function of the VCM in film (v) and the proportion of diet wrapped in film (P).

Table 3

Increased Risk of Malignant Tumors

v		P			
PPM	PPB	.25	.5	.75	1
.001	1	1.29×10^{-7}	2.58×10^{-7}	3.87×10^{-7}	5.17×10^{-7}
.005	5	6.46×10^{-7}	1.29×10^{-6}	1.94×10^{-6}	2.58×10^{-6}
.010	10	1.29×10^{-6}	2.58×10^{-6}	3.87×10^{-6}	5.17×10^{-6}
.050	50	6.46×10^{-6}	1.29×10^{-5}	1.94×10^{-5}	2.58×10^{-5}
.100	100	1.29×10^{-5}	2.58×10^{-5}	3.87×10^{-5}	5.17×10^{-5}
.500	500	6.46×10^{-5}	1.29×10^{-4}	1.94×10^{-4}	2.58×10^{-4}
1.000	1000	1.29×10^{-4}	2.58×10^{-4}	3.87×10^{-4}	5.17×10^{-4}

For example, in a diet consisting of 50% of the food wrapped in film which contains 50 PPM residual VCM, the increased risk of malignant tumors would be 1.29×10^{-5} or a little greater than 1 in 1 hundred thousand.

ppb

In Table 4 various combinations of v and P which result in a 1 in a million increased risk are given.

Table 4

Increased Risk of Malignant Tumors = 10^{-6} as a Function of v and P

P	v: PPM	v: PPB
.25	.008	8
.50	.004	4
.75	.003	3
1	.002	2

(2) Liver Angiosarcomas

Similarly, from the data in Table 1,

$$\Delta R = (8.523 \times 10^{-3})\ D = (1.3552 \times 10^{-5})\ v\ P \qquad (4)$$

$$D = (1.1733 \times 10^{-2})\Delta R \qquad (5)$$

Tables 5, 6 and 7 give the corresponding results for liver angiosarcomas.

Table 5

Increased Risk of Liver Angiosarcomas

	Multi - Stage			Linear Extrapolation
		95%		
ΔR	D (PPM)	LCL	UCL	D
10^{-5}	3.56×10^{-2}	2.59×10^{-2}	4.87×10^{-2}	1.17×10^{-3}
10^{-6}	3.56×10^{-3}	2.59×10^{-3}	4.87×10^{-3}	1.17×10^{-4}
10^{-7}	3.56×10^{-4}	2.59×10^{-4}	4.87×10^{-4}	1.17×10^{-5}

Table 6

Increased Risk of Liver Angiosarcomas

v		P			
PPM	PPB	.25	.5	.75	1
.001	1	3.39×10^{-9}	6.78×10^{-9}	1.02×10^{-8}	1.36×10^{-8}
.005	5	1.69×10^{-8}	3.39×10^{-8}	5.08×10^{-8}	6.78×10^{-8}
.010	10	3.39×10^{-8}	6.78×10^{-8}	1.02×10^{-7}	1.36×10^{-7}
.050	50	1.69×10^{-7}	3.39×10^{-7}	5.08×10^{-7}	6.78×10^{-7}
.100	100	3.39×10^{-7}	6.78×10^{-7}	1.02×10^{-6}	1.36×10^{-6}
.500	500	1.69×10^{-6}	3.39×10^{-6}	5.08×10^{-6}	6.78×10^{-6}
1.000	1000	3.39×10^{-6}	6.78×10^{-6}	1.02×10^{-5}	1.36×10^{-5}

Table 7

Increased Risk of Liver Angiosarcomas = 10^{-6} As a Function of v and P

	v	
P	PPM	PPB
.25	.295	295
.50	.148	148
.75	.098	98
1	.074	74

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