COMPANY CORRESPONDENCE

W. A K

MAY 28 1974

TO DIV: Corporate Environmental Services FROM DIV: Specialty Chemicals

LOCATION: Morristown LOCATION: Buffalo Dye Plant

ATT'N OF: Mr. W. S. Ferguson DATE: May 23, 1974
Director - Occupational Health & Safety

SUBJECT:

VINYL CHLORIDE - PROPOSED OSHA STANDARD

1. Based on Bio-Test/MCA data (Fed. Reg. 39 (92) 16896 (May 10, 1974), we can make the following scale-up and extrapolations assuming a straight-line log dose/probit response.

dose rate	=	50 ppm
respiration rate (mouse)	=	.024 l/min.
respiration rate (man)	=	7.5 l/min.
weight (mouse)	=	.025 Kg
weight (man)	=	70 Kg
incidence rate @ 50 ppm	=	2/200 = .01

upper 99% confidence level of .01 incidence =
.01 + 2.33 (S.D. of the incidence) =

$$.01 + 2.33 \times \sqrt{\frac{.01 \times .99}{200}} = .0264 = \text{probit } 3.06$$

target incidence

10^{-5} = probit .735

10^{-6} = probit .240

10^{-7} = probit -.20

10^{-8} = probit -.62

probit shift to reach targets ($P_{.01}$ - Pt)

10^{-5} Δ p = 2.33

10^{-6} Δ p = 2.82

10^{-7} Δ p = 3.26

10^{-8} Δ p = 3.68

ASI 000010265

1. (Cont'd.)

total dose/mouse =

$$\frac{.024\ l \times 60\ \text{min.} \times 7\ \text{hr.} \times 5\ \text{d.} \times 4.33\ \text{wk.} \times 7\ \text{mo.}}{\text{min.} \times \text{hr.} \times \text{d.} \times \text{wk.} \times \text{mo.}}$$

$$1527.6\ l \text{ or } \times \frac{50}{10^6} = 76.4\ \text{ml of VCM}$$

$$\left(\frac{70}{.025}\right)^{2/3} \times 76.4\ \text{ml} = 15177\ \text{ml VCM}$$

Extrapolation of the log dose/probit line involves the expression

$$\frac{\Delta \log_{10} \text{dose}}{\Delta \text{probit}} = \frac{\Delta \log_{10} D}{\Delta p} = \text{Slope (S)}$$

thus $\Delta \log_{10} D = S\Delta p$

or $\log_{10} D_o - \log_{10} D_1 = S\Delta p$

$$\log_{10} \frac{D_o}{D_1} = S\Delta p \quad \text{or} \quad \frac{D_o}{D_1} = 10^{S\Delta p} \quad \text{or}$$

$$D_1 = D_o \times 10^{-S\Delta p}$$

Mantel-Bryan recommend S = 1 but a more realistic slope may be 0.4. Thus, for various target incidences (acceptable tolerance) and for the alternative slopes, we find

Target Incidence	(S) Selected Slope	(D_1) Calc. Dose (ml)	Calc. conc. VCM in ppm (*)
10^{-5}	1	71	.002
10^{-6}	1	23	.0007
10^{-7}	1	8.3	.00025
10^{-8}	1	3.2	.00009
10^{-5}	0.4	1775	.053
10^{-6}	0.4	1130	.033
10^{-7}	0.4	754	.022
10^{-8}	0.4	512	.015

(*) See next page

(*) In a working lifetime of 40 years, a man inspires

$$\frac{1000\,\text{ml} \times 7.5\,\text{l} \times 60\,\text{min.} \times 8\,\text{hr.} \times 235\,\text{d.} \times 40\,\text{yr.}}{1 \times \text{min.} \times \text{hr.} \times \text{d.} \times \text{yr.}} = 33800 \times 10^6\ \text{ml}$$

Therefore ppm TLV = calc. dose x $10^6/33800 \times 10^6$ = calc. dose/33800

2. This is a discouraging picture and leads one to wonder where the holes in the logic reside. It is important to apply the most realistic slope and this may come out of the present studies. Relative retention rates of man and mouse have not been taken into consideration and this may be important. Most likely to affect the outcome would be quantitative differences in metabolic pathways and immunologic responses.

3. If we extrapolate the data backward, using the above assumptions (slope = 0.4, 99% C.L.), we find that even at 2.7 ppm, the incident rate would be 50%. Since actual VCM may well have long been at this level or higher, there seems to be flaws in the logic or too much built-in conservatism. At a target rate equal to the observed (.01, i.e. $\Delta p = 0$), the TLV for man calculates on the same basis as 0.45 ppm. This is equivalent to saying that man is 100 times as sensitive as a mouse to VCM, an unlikely situation.

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cc: Dr. W. A. Knapp