

**NO SIGNIFICANT RISK LEVELS (NSRLS)  
FOR THE PROPOSITION 65 CARCINOGENS  
METHYLHYDRAZINE AND METHYLHYDRAZINE SULFATE**

**May 2001**

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**SUMMARY OF FINDINGS**

The cancer potencies of methylhydrazine by the oral route and methylhydrazine sulfate were estimated from dose-response data for lung tumors among female mice exposed orally (Toth 1972). The cancer potency estimates correspond to the upper 95 percent confidence bound on the linear term of the multistage model fit to cancer dose-response data in animals.

The cancer potency of methylhydrazine by the inhalation route was estimated from dose-response data for multiple methylhydrazine-responsive tumor sites among female mice exposed by inhalation (Kinkead *et al.*, 1985). These sites were nasal and respiratory mucosa, lung, liver, and blood vessels. For each of these tumor sites, a probability distribution of cancer potency estimates was derived using likelihood theory. The linear term ( $q_1$ ) of the multistage model fit to dose response data for a given site represents the cancer potency for that site. A combined distribution representing cancer potency for all sites affected by methylhydrazine (by the inhalation route) was derived through Monte Carlo analysis. The upper 95 percent confidence bound indicated by the combined distribution for the methylhydrazine-related tumor sites was taken as the cancer potency for inhalation exposures.

The potency derivations take into account body size differences between humans and experimental animals. The Proposition 65 “no significant risk level” (NSRL) is defined in regulation as the daily intake level posing a  $10^{-5}$  lifetime risk of cancer. Cancer potency estimates and the corresponding NSRLs are given in Table 1.

**Table 1. Cancer Potencies and NSRLs for Methylhydrazine and Its Sulfate**

Chemical/Route of Exposure	Cancer Potency (mg/kg-day) <sup>-1</sup>	NSRL ( $\mu$ g/day)
<i>Methylhydrazine</i>		
<i>oral</i>	12	0.058
<i>inhalation</i>	7.8	0.090
<i>Methylhydrazine sulfate</i>	3.8	0.18

**INTRODUCTION**

This report describes the derivation of cancer potency values and NSRLs for methylhydrazine (CAS number 60-34-4, MW = 46.07) and methylhydrazine sulfate (CAS number 5118-34-3, MW =

144.15). “Methylhydrazine and its salts” were listed on July 1, 1992 as chemicals known to the State to cause cancer under Proposition 65 (California Health and Safety Code 25249.5 *et seq.*).

This document discusses the studies available for cancer dose-response assessment, and summarizes the derivations of the cancer potency estimates and NSRLs. A description of the methodology used is provided in the Appendix. Methylhydrazine is primarily used as a rocket propellant, chemical intermediate and solvent (HSDB, 2001).

## **STUDIES SUITABLE FOR DOSE-RESPONSE ASSESSMENT**

Six series of studies investigated the carcinogenic potential of methylhydrazine or methylhydrazine sulfate: five by the oral route (Roe *et al.*, 1967; Kelly *et al.*, 1969; Toth, 1972; Toth and Shimizu, 1973; MacEwen and Vernot, 1975) and one by the inhalation route (Kinkead *et al.*, 1985). The studies of Roe *et al.* (1967) and Kelly *et al.* (1969) were not as suitable for cancer potency estimation as those of Toth (1972), Toth and Shimizu (1973) and Kinkead *et al.* (1985), due to poor survival of the study animals and/or short study duration. A drinking water study in hamsters, MacEwen and Vernot (1975), also was not utilized for cancer potency estimation because no statistically significant increases in tumors were observed.

Toth (1972) treated groups of 50 male and 50 female Swiss mice with either 0.01% methylhydrazine or 0.001% methylhydrazine sulfate in drinking water for life. Controls for the colony of mice used in this study were reported in Toth (1969). The authors calculated average intake of the test substances by male mice over their lifetime to be 0.66 mg/day for methylhydrazine and 0.102 mg/day for the sulfate. The average intake by female mice over their lifetime was calculated to be 0.71 mg/day for methylhydrazine and 0.078 mg/day for the sulfate. Animals were observed until moribund or natural death. The average survival was reduced in methylhydrazine treated mice relative to controls. Treatment with methylhydrazine sulfate did not reduce survival. Treated mice developed lung adenomas and adenocarcinomas. The data are summarized in Table 2.

**Table 2. Lung Tumors in Male and Female Swiss Mice Treated for Life with Methylhydrazine or Its Sulfate via Drinking Water (Toth, 1972)**

Sex, Species	Administered Dose (% in drinking water)	Average Dose <sup>1</sup> (mg/kg-day)	Tumor Incidence <sup>2</sup>	Statistical Significance <sup>3</sup>
<b>Methylhydrazine (MH)</b>				
Male mice	0	0	11/91	--
	0.01	22.0	11/24	p < 0.001
Female mice	0	0	14/107	--
	0.01	28.4	12/39	p = 0.02
<b>MH Sulfate</b>				
Male mice	0	0	11/86	--
	0.001	3.40	23/48	p < 0.001
Female mice	0	0	14/104	--
	0.001	3.12	23/46	p < 0.001

<sup>1</sup> Lifetime average dose is calculated as described in the Appendix.

<sup>2</sup> Control tumor incidences for the colony were reported in Toth (1969). Reported for controls and treated groups are animals with tumor/effective number of animals (i.e., animals alive at first occurrence of tumors in either group).

<sup>3</sup> Results of pairwise comparison using the Fisher Exact Test.

Toth and Shimizu (1973) exposed groups of 50 male and 50 female Syrian golden hamsters to 0.01% methylhydrazine in their drinking water for life. The authors calculated average intake of methylhydrazine to be 1.1 mg/day for males and 1.3 mg/day for females. Control groups of 100 male and 100 female Syrian golden hamsters were maintained concurrently. Animals were observed until moribund or natural death. Increased incidences of malignant histiocytomas of the liver and tumors of the cecum were observed in treated hamsters. The data for the malignant histiocytomas, which showed a more significant increase than the tumors of the cecum, are summarized in Table 3.

**Table 3. Malignant Histiocytomas of the Liver in Male and Female Syrian Golden Hamsters Treated for Life with Methylhydrazine via Drinking Water (Toth and Shimizu, 1973)**

Sex, Species	Administered Dose (% in drinking water)	Average Dose <sup>1</sup> (mg/kg-day)	Tumor Incidence <sup>2</sup>	Statistical Significance <sup>3</sup>
Male hamsters	0	0	0/87	--
	0.01	8.80	27/48	p < 0.001
Female hamsters	0	0	0/92	--
	0.01	11.8	16/47	p < 0.001

<sup>1</sup> Lifetime average dose is calculated as described in the Appendix.

<sup>2</sup> Reported are animals with tumor/effective number of animals (i.e., animals alive at first occurrence of tumors in either group).

<sup>3</sup> Results of pairwise comparison using the Fisher Exact Test.

Kinkead *et al.* (1985) conducted inhalation cancer studies of methylhydrazine on male and female F344 rats, female C57BL/6 mice and male Syrian Golden hamsters. The rodents were exposed to concentrations of 0, 0.02, 0.2, 2.0 or 5.0 ppm methylhydrazine in air for six hours per day, five days per week for 52 weeks. All animals were observed for an additional year before sacrifice.

Methylhydrazine exposure caused a dose-related depression in the growth rate of male rats throughout the entire study. Reduced growth of female rats was only evident in the highest dose group. Among treated hamsters, body weight was reduced in a dose-related manner during the dosing period, but weights normalized during the year-long, post-exposure period. The effect of treatment on the growth of female mice was not reported. No increases in tumors were observed among male or female rats. Among male hamsters, a statistically significant increase in benign nasal tumors (adenomas and polyps) was observed in the two highest dose groups (2.0 and 5.0 ppm) relative to controls ( $p<0.05$ ). Among female mice, dose-related increases in lung adenoma and carcinoma, liver adenoma and carcinoma, and hemangioma were observed relative to controls (Table 4). A dose-related increase in nasal tumors, significant only by trend test, was also observed (Table 4).

Kinkead *et al.* (1985) reported benign and malignant tumor incidences separately, making it unclear whether the benign or malignant tumors occurred in separate animals or whether some of the animals exhibited both benign and malignant tumors. The possible range of incidences of combined benign and malignant tumors for liver, lung, and blood vessels are shown in italics in Table 4, based on the female mouse data reported by Kinkead *et al.* (1985).

**Table 4. Neoplastic Lesions in Female C57Bl/6 Mice Treated for One Year with Methylhydrazine via Inhalation (Kinkead *et al.*, 1985)**

Administered dose (ppm) <sup>1</sup>	Controls	0.02	0.2	2.0	trend <sup>3</sup>
Average dose <sup>2</sup> (mg/kg-d)	0	0.0058	0.058	0.58	
<u>Tumor site</u>					
Nasal and respiratory mucosa (benign)	0/367	2/354	1/349	4/355	p = 0.02
Lung adenoma	13/364	16/354	23/347 <sup>4</sup>	56/360 <sup>4</sup>	p < 0.0001
Lung carcinoma	0/364	4/354	2/347	3/360	p = 0.28
<i>Lung adenoma/carcinoma combined (possible range)</i>	<i>13/364</i>	<i>16-20/354</i>	<i>23-25/347<sup>4</sup></i>	<i>56-59/360<sup>5</sup></i>	<i>p &lt; 0.0001</i>
Liver adenoma	6/373	2/357	5/357	20/363 <sup>5</sup>	p < 0.0001
Liver carcinoma	2/373	4/357	4/357	14/363 <sup>5</sup>	p < 0.0001
<i>Liver adenoma/carcinoma combined (possible range)</i>	<i>6-8/373</i>	<i>4-6/357</i>	<i>5-9/357</i>	<i>20-34/363<sup>5</sup></i>	<i>p &lt; 0.0001</i>
Duodenum adenoma	1/310	5/303	7/309 <sup>5</sup>	5/308	p = 0.34
Hemangioma	5/387	9/371	5/368	22/371 <sup>5</sup>	p < 0.0001
Hemangiosarcoma	1/387	4/371	4/368	5/371	p = 0.15
<i>Hemangioma/-sarcoma combined (possible range)</i>	<i>5-6/387</i>	<i>9-13/371</i>	<i>5-9/368</i>	<i>22-27/371<sup>5</sup></i>	<i>p &lt; 0.0001</i>

<sup>1</sup> Methylhydrazine was administered 6 hours per day, 5 days per week for 52 weeks.

<sup>2</sup> Lifetime average dose is calculated as described in the Appendix.

<sup>3</sup> Mantel-Haenszel trend test.

<sup>4</sup> Significantly different from control animals by pairwise Fisher Exact Test, p < 0.05.

<sup>5</sup> Significantly different from control animals by pairwise Fisher Exact Test, p < 0.01.

## APPROACH TO DOSE RESPONSE ANALYSIS

Methylhydrazine is mutagenic in some strains of bacteria (CCCRIS, 2000). These findings suggest that a genotoxic mode of action is plausible. There is insufficient information on the precise mechanism of carcinogenicity to permit the development of a biologically based model for cancer potency estimation. There are also insufficient data to support dose adjustments based on pharmacokinetic models. Therefore, the default approach (i.e., a linearized multistage model and interspecies scaling) has been applied. The approach used is described in detail in the Appendix.

## DOSE-RESPONSE ASSESSMENT

Cancer potency estimates derived from studies employing oral exposures are summarized in Table 5. Methylhydrazine was tested in both hamsters and mice, while methylhydrazine sulfate was tested in mice

only. This assessment assumes that the methylhydrazine cation is the active agent responsible for inducing tumors in these experiments.

**Table 5. Human Cancer Potency Estimates for Methylhydrazine and Methylhydrazine Sulfate for Oral Exposures**

	Methylhydrazine Cancer Potency Estimate (mg/kg-day) <sup>-1</sup>	Methylhydrazine Sulfate Cancer Potency Estimate (mg/kg-day) <sup>-1</sup>
Toth (1972)		
<i>Male Swiss mice</i>	0.51	3.0
<i>Female Swiss mice</i>	0.22	<b>3.8<sup>1</sup></b>
Toth and Shimizu (1973)		
<i>Male Syrian golden hamsters</i>	1.1	--
<i>Female Syrian golden hamsters</i>	0.45	--

<sup>1</sup> Bolding indicates value selected as the basis of the NSRL (oral exposures).

Based on a molecular weight comparison and an assumption that methylhydrazine (or methylhydrazine cation) is the active chemical species, one would predict the potency of methylhydrazine to be greater than that of the sulfate salt. However, the potencies derived from the Toth (1972) studies indicate that the sulfate salt is more potent in mice under the experimental conditions employed. In discussing the non-intuitive relative potencies derived from the Toth (1972) studies, NIOSH (1978) discussed the possibility that free methylhydrazine was less stable than the sulfate salt in water, citing a study which showed that a solution of unbuffered methylhydrazine in water degraded by 60% in 24 hours. Toth (1972) and Toth and Shimizu (1973) did not specify whether or not the methylhydrazine drinking water solution was buffered. Therefore, in these studies, the actual doses administered to the animals may have been less than those reported by the authors, resulting in an underestimate of the cancer potency for methylhydrazine. Alternatively, since methylhydrazine was administered at a dose ten times higher than that of methylhydrazine sulfate in the studies by Toth (1972), the observed reduced survival of the methylhydrazine-treated animals may have reduced the observed tumor response. The lung tumor response of female mice to methylhydrazine sulfate (Toth, 1972) is identified as the most sensitive tumor response for either compound administered by the oral route, yielding a cancer potency estimate of 3.8 (mg/kg-d)<sup>-1</sup>. The potency estimate for methylhydrazine by the oral route is 12 (mg/kg-d)<sup>-1</sup> after rounding, based on a molecular weight conversion from the potency derived for methylhydrazine sulfate [3.8 (mg/kg-d)<sup>-1</sup> \* (144.15/46.07)].

Cancer potency estimates of methylhydrazine derived from studies of inhalation exposures in mice are summarized in Table 6. Mice were more sensitive to the effects of methylhydrazine than hamsters or rats (Kinkead *et al.*, 1985). Potency estimates were derived for tumor sites in the mice exhibiting statistically significant dose-dependent responses as shown in Table 4. As discussed earlier, benign and malignant tumor incidences were reported by Kinkead *et al.* (1985), thus it is unclear whether the benign or malignant tumors occurred in separate animals or whether some of the animals exhibited both

benign and malignant tumors (Table 4). In order to determine the possible range of potency estimates for combined benign and malignant tumors at a given site, datasets for combined incidences of benign and malignant tumors of the liver, lung, and blood vessels were generated based on three different sets of assumptions. In the first case, the reported benign and malignant tumors were assumed to occur in the same animals. In the second case, the reported benign and malignant tumors were assumed to occur in different animals. In the third case, the reported benign and malignant tumors were assumed to occur in the same animals in the control groups, but those reported in the treated groups were assumed to occur in different animals. Table 6 presents the range of potency estimates derived from these datasets for each of the relevant target sites.

Also, Kinkead *et al.* (1985) exposed the mice for one year and sacrificed the animals at two years of age. The less than lifetime dosing reduces the sensitivity of the assay and could potentially lead to an underestimation of cancer risk compared to lifetime exposure. To account for this short exposure duration, the administered doses were averaged over the two-year experimental duration. This approach may not adequately adjust the potency estimate; there is the possibility that the true risks from chronic exposures to methylhydrazine may be underpredicted.

**Table 6. Human Cancer Potency Estimates for Methylhydrazine Inhalation Exposures (Kinkead *et al.* (1985), female B57BL/6 mice)**

Tumor site	Methylhydrazine Cancer Potency Estimate (mg/kg-day) <sup>-1</sup>
Nasal and respiratory mucosa (benign) <sup>1</sup>	0.51
Lung adenoma Lung adenoma/carcinoma (combined) <sup>1,2</sup>	4.2 4.2 to 4.3
Liver adenoma Liver carcinoma Liver adenoma/carcinoma (combined) <sup>1,2</sup>	1.7 1.3 1.6 to 2.8
Hemangioma Hemangioma/-sarcoma (combined) <sup>1,2</sup>	1.6 1.6 to 1.9
All methylhydrazine-related tumor sites	<b>7.8</b>

Bolding indicates value selected as the basis of the NSRL (inhalation exposures).

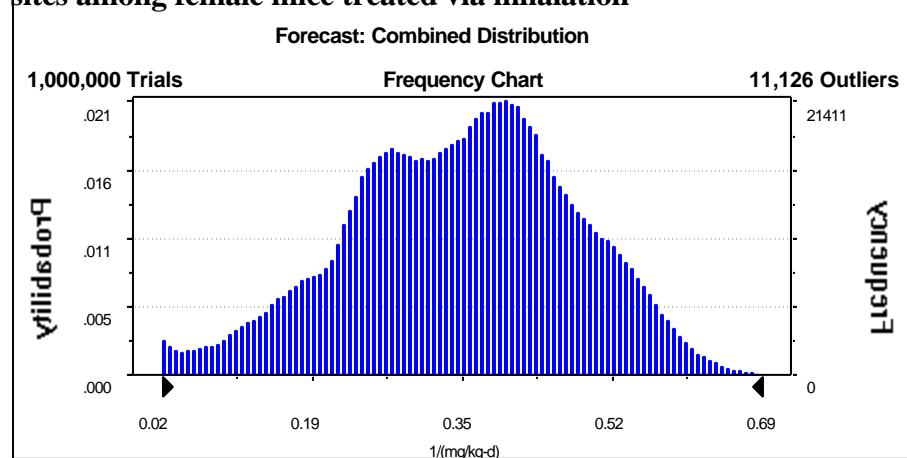
<sup>1</sup> Distributions of  $q_1$  combined using Monte Carlo analysis (e.g., "all methylhydrazine-related tumor sites").

<sup>2</sup> Range of potency estimates based on various assumptions of whether the reported benign and malignant tumors occurred in the same animals or different animals (see text).

Since methylhydrazine induced tumors at multiple sites in female mice, a combined potency estimate for all treatment-related tumor sites was derived using Monte Carlo analysis. For each tumor site, a distribution of estimates corresponding to the 0.1 through 99.9 percentiles of the linear term ( $q_1$ ) of the multistage model was generated with the MSTAGE 2.01 computer program (created by Edmund Crouch), which had been modified to tabulate percentile values. A combined distribution (Figure 1) was created by adding  $q_1$  for each tumor site, according to its distribution, through one million Monte Carlo trial simulations (Crystal Ball 2000 software, Decisioneering, Inc., Denver, Colorado). The upper 95 percent confidence bound of the combined distribution was taken as the basis of the cancer potency estimate for the combined tumor sites (Table 6).

Distributions of the cancer potency estimates were combined for the following tumor sites: nasal and respiratory mucosa (benign), lung adenoma and carcinoma (combined), liver adenoma and carcinoma (combined), and hemangioma and hemangiosarcoma (combined) (Figure 1). Datasets for lung, liver and blood vessel tumors assumed that benign and malignant tumors occurred in different animals (case 2 as described above).

**Figure 1. Combined distribution of potency estimates for all methylhydrazine-related tumor sites among female mice treated via inhalation**



The upper 95 percent confidence bound of the combined analysis (Figure 1) yielded an animal cancer potency of  $0.55 \text{ (mg/kg}\text{-}d)^{-1}$ . Using methods described in the Appendix, this estimate was scaled to a human-equivalent cancer potency estimate of  $7.8 \text{ (mg/kg}\text{-}d)^{-1}$ , which was selected as the basis of the NSRL for inhalation exposures to methylhydrazine.

## NO SIGNIFICANT RISK LEVEL

The NSRL for Proposition 65 is the intake associated with a lifetime cancer risk of  $10^{-5}$ . The most sensitive cancer potency estimate for oral exposures (Table 5) was used to calculate the NSRL for methylhydrazine by the oral route as  $0.058 \mu\text{g/day}$  and the NSRL for methylhydrazine sulfate as  $0.18 \mu\text{g/day}$ . The combined cancer potency estimate for all methylhydrazine-related tumors from inhalation

exposures (Table 6) was used to calculate the NSRL for methylhydrazine by the inhalation route as 0.090 µg/day.

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## **APPENDIX: DEFAULT METHODOLOGY USED TO DERIVE NSRLS FOR METHYLHYDRAZINE AND METHYLHYDRAZINE SULFATE**

Procedures for the development of Proposition 65 NSRLs are described in regulation (California Code of Regulations, Title 22, Sections 12701 and 12703). Consistent with these procedures, the specific methods used to derive the NSRLs for methylhydrazine and methylhydrazine sulfate are outlined in this Appendix.

### **A.1 Cancer Potency as Derived from Animal Data**

#### **"Multistage" polynomial**

For regulatory purposes, the lifetime probability of dying with a tumor ( $p$ ) induced by an average daily dose ( $d$ ) is often assumed to be (CDHS, 1985; U.S. EPA, 1996; Anderson *et al.*, 1983):

$$p(d) = 1 - \exp[-(q_0 + q_1d + q_2d^2 + \dots + q_jd^j)] \quad (1)$$

with constraints,

$$q_i \geq 0 \text{ for all } i.$$

The  $q_i$  are parameters of the model, which are taken to be constants and are estimated from the data. The parameter  $q_0$  represents the background lifetime incidence of the tumor. The parameter  $q_1$ , or some upper bound, is often called the cancer potency, since for small doses it is the ratio of excess lifetime cancer risk to the average daily dose received. For the present discussion, cancer potency will be defined as  $q_1^*$ , the upper 95% confidence bound on  $q_1$  (CDHS, 1985), estimated by maximum likelihood techniques. When dose is expressed in units of mg/kg-day, the parameters  $q_1$  and  $q_1^*$  are given in units of  $(\text{mg/kg-day})^{-1}$ . Details of the estimation procedure are given in Crump (1981) and Crump *et al.* (1977). To estimate potency in animals ( $q_{\text{animal}}$ ) from experiments of duration  $T_e$ , rather than the natural life span of the animals ( $T$ ), it is assumed that the lifetime incidence of cancer increases with the third power of age:

$$q_{\text{animal}} = q_1^* \cdot (T/T_e)^3 \quad (2)$$

Following Gold and Zeiger (1997) and the U.S. Environmental Protection Agency (U.S. EPA, 1988), the natural life span of mice and rats is assumed to be two years, so that for experiments lasting  $T_e$  weeks in these rodents:

$$q_{\text{animal}} = q_1^* \cdot (104/T_e)^3 \quad (3)$$

To estimate risk at low doses, potency is multiplied by average daily dose. The risk estimate obtained is referred to by the U.S. EPA (Anderson *et al.*, 1983) as "extra risk", and is equivalent to that obtained by using the Abbott (1925) correction for background incidence.

For inhalation exposures to methylhydrazine, cancer potency is taken as the upper 95 percent confidence bound for the multiple sites affected by methylhydrazine administered by the inhalation route. The methods to estimate the combined distribution are described in the main text (pp. 5-7).

### **Calculation of the lifetime average dose**

The lifetime average doses in units of mg/kg-day for the studies used to derive potency estimates were as follows. In the drinking water studies, Toth (1972) reported average methylhydrazine intakes of 0.66 mg/day for male mice and 0.71 mg/day for females. For methylhydrazine sulfate, Toth (1972) reported average intakes of 0.102 mg/day for male mice and 0.078 mg/day for females. Lifetime average doses were calculated by dividing the intake by the default body weight (0.03 kg for male mice and 0.025 kg for female mice; Gold and Zeiger, 1997). Toth and Shimizu (1973) reported average methylhydrazine intake to be 1.1 mg/day for male Syrian Golden hamsters and 1.3 mg/day for females. Lifetime average doses were calculated by dividing the intake by the default body weights (0.125 kg for male hamsters and 0.110 kg for female hamsters; Gold and Zeiger, 1997). In the inhalation study of methylhydrazine, female mice were exposed 6 hours per day, 5 days per week for 52 weeks and sacrificed after an additional year of observation. The air concentrations of methylhydrazine in units of ppm were converted to lifetime average dose in units of mg/kg-d as shown in the following equation.

$$\left(\frac{\text{parts}}{1,000,000 \text{ parts}}\right)\left(\frac{46.07 \text{ g/mol}}{24.45 \text{ L/mol}}\right)\left(\frac{1000 \text{ mg}}{\text{g}}\right)\left(\frac{0.03 \text{ L}}{\text{min}}\right)\left(\frac{60 \text{ min}}{\text{h}}\right)\left(\frac{6 \text{ h}}{\text{d}}\right)\left(\frac{5 \text{ d}}{\text{wk}}\right)\left(\frac{52 \text{ wk}}{\text{yr}}\right)\left(\frac{1}{0.025 \text{ kg}}\right)\left(\frac{\text{yr}}{2 * 365 \text{ d}}\right) = \frac{\text{mg}}{\text{kg-d}}$$

The default inhalation rate (0.03 L/min), body weight (0.025 kg) and lifespan (2 years) for female mice were those reported by Gold and Zeiger (1997). The value 46.07 g/mol is the molecular weight of methylhydrazine, and the value 24.45 L/mol is the molar gas constant at 25°C.

### **A.2 Interspecies Scaling**

Once a potency value is estimated in animals following the techniques described above, human potency is estimated. As described in the California risk assessment guidelines (CDHS, 1985), a dose in units of milligram per unit surface area is assumed to produce the same degree of effect in different species in the absence of information indicating otherwise. Under this assumption, scaling to the estimated human potency ( $q_{\text{human}}$ ) can be achieved by multiplying the animal potency ( $q_{\text{animal}}$ ) by the ratio of human to animal body weights ( $bw_h/bw_a$ ) raised to the one-third power when animal potency is expressed in units (mg/kg-day)<sup>-1</sup>:

$$q_{\text{human}} = q_{\text{animal}} \cdot (bw_h / bw_a)^{1/3} \quad (4)$$

### **A.3 Risk-Specific Intake Level Calculation**

The intake level (I, in mg/day) associated with a cancer risk R, from exposure is:

$$I = \frac{R \cdot bw_h}{q_{\text{human}}} \quad (5)$$

where  $bw_h$  is the body weight, and  $q_{\text{human}}$  the theoretical cancer potency estimate for humans.

Daily intake levels associated with lifetime cancer risks above  $10^{-5}$  exceed the no significant risk level for cancer under Proposition 65 (Title 22 California Code of Regulations, Section 12703).

Thus for a 70 kg person, the NSRL is given by:

$$\text{NSRL} = \frac{10^{-5} \cdot 70\text{kg}}{q_{\text{human}}} \quad (6)$$

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