APPENDIX A. ATSDR MINIMAL RISK LEVELS AND WORKSHEETS

The Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) [42 U.S.C. 9601 et seq.], as amended by the Superfund Amendments and Reauthorization Act (SARA) [Pub. L. 99–499], requires that the Agency for Toxic Substances and Disease Registry (ATSDR) develop jointly with the U.S. Environmental Protection Agency (EPA), in order of priority, a list of hazardous substances most commonly found at facilities on the CERCLA National Priorities List (NPL); prepare toxicological profiles for each substance included on the priority list of hazardous substances; and assure the initiation of a research program to fill identified data needs associated with the substances.

The toxicological profiles include an examination, summary, and interpretation of available toxicological information and epidemiologic evaluations of a hazardous substance. During the development of toxicological profiles, Minimal Risk Levels (MRLs) are derived when reliable and sufficient data exist to identify the target organ(s) of effect or the most sensitive health effect(s) for a specific duration for a given route of exposure. An MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. MRLs are based on noncancer health effects only and are not based on a consideration of cancer effects. These substance-specific estimates, which are intended to serve as screening levels, are used by ATSDR health assessors to identify contaminants and potential health effects that may be of concern at hazardous waste sites. It is important to note that MRLs are not intended to define clean-up or action levels.

MRLs are derived for hazardous substances using the no-observed-adverse-effect level/uncertainty factor approach. They are below levels that might cause adverse health effects in the people most sensitive to such chemical-induced effects. MRLs are derived for acute (1–14 days), intermediate (15–364 days), and chronic (365 days and longer) durations and for the oral and inhalation routes of exposure. Currently, MRLs for the dermal route of exposure are not derived because ATSDR has not yet identified a method suitable for this route of exposure. MRLs are generally based on the most sensitive chemical-induced end point considered to be of relevance to humans. Serious health effects (such as irreparable damage to the liver or kidneys, or birth defects) are not used as a basis for establishing MRLs. Exposure to a level above the MRL does not mean that adverse health effects will occur.

MRLs are intended only to serve as a screening tool to help public health professionals decide where to look more closely. They may also be viewed as a mechanism to identify those hazardous waste sites that

are not expected to cause adverse health effects. Most MRLs contain a degree of uncertainty because of the lack of precise toxicological information on the people who might be most sensitive (e.g., infants, elderly, nutritionally or immunologically compromised) to the effects of hazardous substances. ATSDR uses a conservative (i.e., protective) approach to address this uncertainty consistent with the public health principle of prevention. Although human data are preferred, MRLs often must be based on animal studies because relevant human studies are lacking. In the absence of evidence to the contrary, ATSDR assumes that humans are more sensitive to the effects of hazardous substance than animals and that certain persons may be particularly sensitive. Thus, the resulting MRL may be as much as 100-fold below levels that have been shown to be nontoxic in laboratory animals.

Proposed MRLs undergo a rigorous review process: Health Effects/MRL Workgroup reviews within the Division of Toxicology and Human Health Sciences (proposed), expert panel peer reviews, and agency-wide MRL Workgroup reviews, with participation from other federal agencies and comments from the public. They are subject to change as new information becomes available concomitant with updating the toxicological profiles. Thus, MRLs in the most recent toxicological profiles supersede previously published levels. For additional information regarding MRLs, please contact the Division of Toxicology and Human Health Sciences (proposed), Agency for Toxic Substances and Disease Registry, 1600 Clifton Road NE, Mailstop F-62, Atlanta, Georgia 30333.

APPENDIX A

MINIMAL RISK LEVEL (MRL) WORKSHEET

Chemical Name: Vanadium compounds
CAS Numbers: 7440-62-2
Date: July 2012
Profile Status: Post-Public Comment, Third Draft
Route: [X] Inhalation [ ] Oral
Duration: [X] Acute [ ] Intermediate [ ] Chronic
Graph Key: 4
Species: Rat

Minimal Risk Level: 0.0008 [ ] mg/kg/day [X] mg vanadium/m^3

Reference: NTP. 2002. NTP toxicology and carcinogenesis studies of vanadium pentoxide (CAS No. 1314-62-1) in F344/N rats and B6C3F1 mice (inhalation). Natl Toxicol Program Tech Rep Ser (507):1-343.

Experimental design: Groups of 40–60 female F344 rats were exposed to 0, 1, 2, or 4 mg vanadium pentoxide/m^3 (0, 0.56, 1.1, and 2.2 mg vanadium/m^3) 6 hours/day, 5 days/week for 16 days. On days 6 and 13, 10 rats/group were killed and a histopathological examination of the lungs was conducted. Four animals per group were killed for examination of onset and extent of lung lesions on days 1, 2, 5, 10, and 16. The remaining animals were used to measure blood and lung concentrations of vanadium, lung clearance half-times, and cell proliferation rates.

Effect noted in study and corresponding doses: Hyperplasia of alveolar epithelium and bronchiole epithelium were observed in 100% of the female rats exposed to 1.1 or 2.2 mg vanadium/m^3 for 6 or 13 days. Significant increases in the incidence of histiocytic infiltrate and inflammation were observed in rats exposed to 1.1 or 2.2 mg vanadium/m^3 for 6 or 13 days and in rats exposed to 0.56 mg vanadium/m^3 for 13 days. A significant increase in fibrosis was observed in rats exposed to 2.2 mg vanadium/m^3 for 13 days. No histopathological alterations were observed in the four female rats killed after 1 day of exposure; by day 2, inflammation and histiocytic infiltrates (increased number of alveolar macrophages) were observed in the rats exposed to 2.2 mg vanadium/m^3. Hyperplasia of the alveolar and bronchiolar epidthelium was first observed on day 5 in rats exposed to 1.1 or 2.2 mg vanadium/m^3.

Dose and end point used for MRL derivation: Increase in the incidence of lung inflammation in rats exposed to 0.56 mg vanadium/m^3 as vanadium pentoxide for 13 days; the human equivalent concentration of this LOAEL ($LOAEL_{HEC}$) is 0.073 mg vanadium/m^3.

[ ] NOAEL [X] LOAEL

A BMD analysis was considered for determining the point of departure for the inflammation in female rats exposed to vanadium pentoxide for 13 days. All available dichotomous models in the EPA benchmark dose software ([BMDS] version 2.1) were fit to the incidence data for lung inflammation (0/10, 8/10, 10/10, and 10/10 in rats exposed to 0, 0.56, 1.1, or 2.2 mg vanadium/m^3) using the extra risk option. The multistage model was run for all polynomial degrees up to n-1 (where n is the number of dose groups including control). Adequate model fit is judged by three criteria: goodness-of-fit p-value ($p>0.1$), visual inspection of the dose-response curve, and scaled residual at the data point (except the control) closest to the predefined benchmark response (BMR). Among all the models providing adequate fit to the data, the lowest lower bound on the BMC (BMCL) is selected as the point of departure when the difference between the BMDLs estimated from these models are more than three-fold; otherwise, the BMCL from the model with the lowest AIC is chosen. In accordance with U.S. EPA (2000) guidance,

benchmark concentrations (BMCs) and BMCLs associated with an extra risk of 10% are calculated for all models.

Table A-1. Model Predictions for the Incidence of Inflammation in Female Rats Exposed to Vanadium Pentoxide 6 Hours/Day, 5 Days/Week for 13 Days

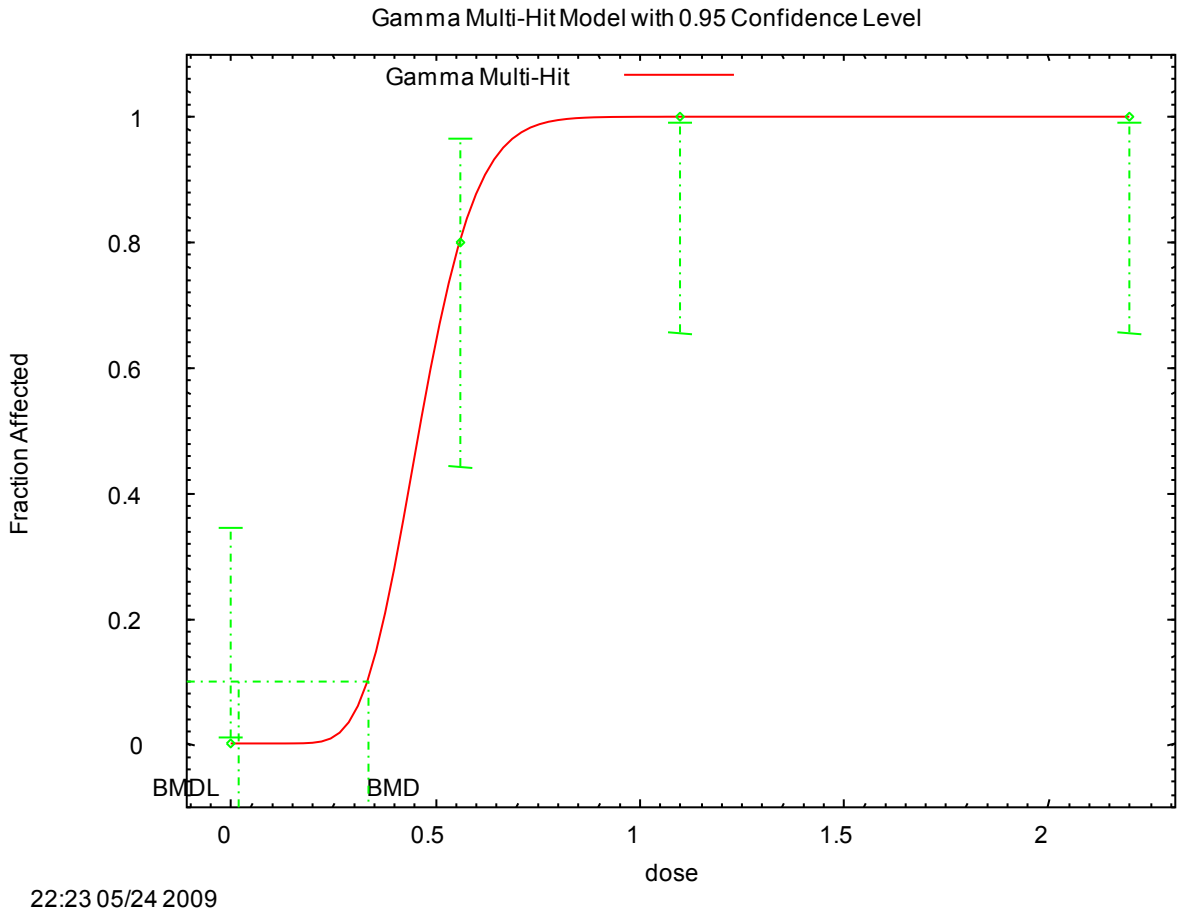
Model	χ^2 Goodness of fit p-value[a]	AIC	BMC_{10} (mg V/m^3)	$BMCL_{10}$ (mg V/m^3)
Gamma[b]	**1.00**	**12.01**	**0.33**	**0.02**
Logistic	1.00	14.01	0.46	0.10
LogLogistic	1.00	12.01	0.46	0.01
LogProbit	1.00	14.01	0.42	0.03
Multistage[c]	0.93	12.69	0.03	0.02
Probit	1.00	14.01	0.38	0.09
Weibull[b]	1.00	14.01	0.25	0.02
Quantal-linear	0.93	12.69	0.03	0.02

[a]Values <0.10 fail to meet conventional goodness-of-fit criteria
[b]Power restricted to ≥1
[c]Betas restricted to ≥0; 1-degree polynomial

AIC = Akaike Information Criterion; BMC = maximum likelihood estimate of the concentration associated with the selected benchmark response; BMCL = 95% lower confidence limit on the BMC

Source: NTP 2002

Figure A-1. Fit of Gamma Model to Data on the Incidence of Inflammation in Female Rats Exposed to Vanadium Pentoxide for 13 Days



BMCs and BMCLs indicated are associated with an extra risk of 10%, and are in units of mg vanadium/m^3

Source: NTP 2002

Although the data provide an adequate statistical fit, the estimated $BMCL_{10}$ of 0.02 mg vanadium/m^3 appears to be an overly conservative estimate of a no-adverse-effect level, which may be a reflection of the limited amount of information from the study on the shape of the exposure-response relationship (incidences of lung inflammation were 0/10 in controls and 8/10 at the lowest vanadium concentration). In a chronic-duration study conducted by NTP (2002), no significant alterations in the incidence of lung inflammation were observed in male and female rats exposed to 0.28 mg vanadium/m^3; the LOAEL for lung inflammation was 0.56 mg vanadium/m^3 in males and 1.1 mg vanadium/m^3 in females.

Due to the low confidence in the $BMCL_{10}$, a NOAEL/LOAEL approach was used to determine the point of departure for the acute MRL.

Uncertainty Factors used in MRL derivation:

[X] 3 for use of a minimal LOAEL
[X] 3 for extrapol

0.ation from animals to humans with dosimetric adjustment
[X] 10 for human variability

Was a conversion factor used from ppm in food or water to a mg/body weight dose? Not applicable.

If an inhalation study in animals, list conversion factors used in determining human equivalent dose:

The duration-adjusted LOAEL of 0.1 mg vanadium/m^3 was converted to a human equivalent concentration ($LOAEL_{HEC}$) using the following equation:

$$LOAEL_{HEC} = LOAEL_{ADJ} \times RDDR_{TH}$$
$$LOAEL_{HEC} = 0.1 \text{ mg vanadium/m}^3 \times 0.732$$
$$LOAEL_{HEC} = 0.073 \text{ mg vanadium/m}^3$$

where:
The RDDR is a multiplicative factor used to adjust an observed inhalation particulate exposure concentration of an animal to the predicted inhalation particulate exposure concentration for a human. The RDDR program (EPA 1990) was used to calculate a multiplier of 0.732 for the thoracic region was determined using a default body weight of 0.124 kg (EPA 1994c) and a particle size MMAD of 1.2 µm with a geometric standard deviation of 1.9

Was a conversion used from intermittent to continuous exposure? The LOAEL was adjusted for intermittent exposure as follows:

$$LOAEL_{ADJ} = LOAEL \times 6 \text{ hours/day} \times 5 \text{ days/week}$$
$$LOAEL_{ADJ} = 0.56 \text{ mg vanadium/m}^3 \times 6 \text{ hours/24 hours} \times 5 \text{ days/7 days}$$
$$LOAEL_{ADJ} = 0.1 \text{ mg vanadium/m}^3$$

Other additional studies or pertinent information that lend support to this MRL: Data on acute toxicity of vanadium in humans are limited to an experimental study in which a small number of subjects were exposed to vanadium pentoxide dust for 8 hours (Zenz and Berg 1967). A persistent cough lasting for 8 days developed in two subjects exposed to 0.6 mg vanadium/m^3; at 0.1 mg vanadium/m^3, a productive cough without any subjective complaints or impact on work or home activities were observed in 5 subjects. The available studies in laboratory animals focused on potential respiratory tract effects. Impaired lung function characterized as airway obstructive changes (increased resistance and decreased airflow) were observed in monkeys exposed to 2.5 or 1.7 mg vanadium/m^3 as vanadium pentoxide for 6 hours (Knecht et al. 1985, 1992); the highest NOAEL for this effect was 0.34 mg vanadium/m^3. Alveolar and bronchiolar epithelial hyperplasia and inflammation were observed in the lungs of mice exposed to 1.1 mg vanadium/m^3 6 hours/day, 5 days/week for 13 days (NTP 2002). Although the Knecht et al. (1985, 1992) or NTP (2002) studies did not include examination of potential end points outside of the respiratory tract, longer-duration studies have identified the respiratory tract as the most sensitive target of toxicity (NTP 2002).

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APPENDIX A

MINIMAL RISK LEVEL (MRL) WORKSHEET

Chemical Name: Vanadium compounds
CAS Numbers: 7440-62-2
Date: July 2012
Profile Status: Post-Public Comment, Third Draft
Route: [X] Inhalation [ ] Oral
Duration: [ ] Acute [ ] Intermediate [X] Chronic
Graph Key: 19
Species: Rat

Minimal Risk Level: 0.0001 [ ] mg/kg/day [X] mg vanadium/m^3

Reference: NTP. 2002. NTP toxicology and carcinogenesis studies of vanadium pentoxide (CAS No. 1314-62-1) in F344/N rats and B6C3F1 mice (inhalation). Natl Toxicol Program Tech Rep Ser (507):1-343.

Experimental design: Groups of 50 male and 50 female F344 rats were exposed to 0, 0.5, 1, or 2 mg vanadium pentoxide/m^3 (0, 0.28, 0.56, and 1.1 mg vanadium/m^3) 6 hours/day, 5 days/week for 104 weeks. The following parameters were used to assess toxicity: clinical observations, body weights (every 4 weeks from week 5 to 89 and every 2 weeks from week 92 to 104), complete necropsy, and microscopic examination of major tissues and organs.

Effect noted in study and corresponding doses: No significant alterations in survival or body weight gain were observed in the vanadium-exposed rats. A summary of selected non-neoplastic respiratory tract lesions is presented in Table A-2. Alveolar histiocytic infiltrates were observed in males and females exposed to ≥0.28 mg vanadium/m^3. Significant increases in the incidence of hyperplasia of the alveolar and bronchiolar epithelium were observed in males exposed to ≥0.28 mg vanadium/m^3 and females exposed to ≥0.56 mg vanadium/m^3. Squamous metaplasia was observed in alveolar epithelium of males and females exposed to 1.1 mg vanadium/m^3 and in the bronchiolar epithelium of males exposed to 1.1 mg vanadium/m^3. Chronic inflammation was observed in males exposed to 0.56 or 1.1 mg vanadium/m^3 and females exposed to 1.1 mg vanadium/m^3 and interstitial fibrosis was observed in males exposed to 1.1 mg vanadium/m^3 and females exposed to 0.28 or 1.1 mg vanadium/m^3. An increased incidence of brownish pigment in alveolar macrophages was observed in males exposed to 1.1 mg vanadium/m^3 and females exposed to 0.56 or 1.1 mg vanadium/m^3; this effect was considered to be of little biological relevance. Chronic inflammation, degeneration, and hyperplasia of the epiglottis were observed in the larynx of males and females exposed to ≥0.28 mg vanadium/m^3; squamous metaplasia of the epiglottis respiratory epithelium was also observed in males exposed to ≥0.28 mg vanadium/m^3 and in females exposed to 1.1 mg vanadium/m^3. Goblet cell hyperplasia of the nasal respiratory epithelium was observed in males exposed to ≥0.28 mg vanadium/m^3 and in females exposed to 1.1 mg vanadium/m^3. A positive trend for increased incidences of uterine stromal polyp was observed; NTP did not consider it to be related to vanadium pentoxide exposure. An increased incidence of nephropathy was observed in male rats exposed to 0.56 or 1.1 mg vanadium/m^3; NTP considered the finding to be of marginal biological significance because there was a lack of increase in severity, as compared to controls, and significant findings in female rats. No significant increases in the incidence of lung neoplasms were observed; however, the incidence of alveolar/bronchiolar adenoma in males exposed to 0.28 mg vanadium/m^3 and alveolar/bronchiolar carcinoma or combined incidence of adenoma and carcinoma in males exposed to 0.28 or 1.1 mg vanadium/m^3 were higher than historical controls. These increases in lung tumors were considered to be related to vanadium pentoxide exposure.

Table A-2. Selected Respiratory Tract Effects Observed in Rats Exposed to Vanadium Pentoxide 6 Hours/Day, 5 Days/Week for 2 Years

Air concentration (mg vanadium/m^3)	0	0.28	0.56	1.1
Males				
Lungs				
Alveolar hyperplasia	7/50 (2.3)	24/49[b] (2.0)	34/48[b] (2.0)	49/50[b] (3.3)
Bronchiole hyperplasia	3/50 (2.3)	17/49[b] (2.2)	31/48[b] (1.8)	49/50[b] (3.3)
Inflammation	5/50 (1.6)	8/49 (1.8)	24/48[b] (1.3)	42/50[b] (2.4)
Fibrosis	7/50 (1.4)	7/49 (2.0)	16/48[c] (1.6)	38/50[b] (2.1)
Histiocyte infiltration	22/50 (1.3)	40/49[b] (2.0)	45/48[b] (2.3)	50/50[b] (3.3)
Larynx				
Chronic inflammation	3/49 (1.0)	20/50[b] (1.1)	17/50[b] (1.5)	28/49[b] (1.6)
Degeneration of epiglottis respiratory epithelium	0/49	22/50[b] (1.1)	23/50[b] (1.1)	33/50[b] (1.5)
Hyperplasia of epiglottis respiratory epithelium	0/49	22/50[b] (1.1)	23/50[b] (1.1)	33/49[b] (1.5)
Squamous metaplasia of epiglottis respiratory epithelium	0/49	18/50[b] (1.5)	34/50[b] (1.5)	32/49[b] (1.9)
Nose				
Hyperplasia of respiratory epithelium goblet cell	4/49 (1.8)	15/50[b] (1.8)	12/49[c] (2.0)	17/48[b] (2.1)
Female				
Lung				
Alveolar hyperplasia	4/49 (1.0)	8/49 (1.8)	21/50[b] (1.2)	50/50[b] (3.1)
Bronchiole hyperplasia	6/49 (1.5)	5/49 (1.6)	14/50[c] (1.3)	48/50[b] (3.0)
Inflammation	10/49 (1.5)	10/49 (1.1)	14/50 (1.2)	40/50[c] (1.7)
Fibrosis	19/49 (1.4)	7/49 (1.3)	12/50 (1.6)	32/50[b] (1.4)
Histiocyte infiltration	26/49 (1.4)	35/49[c] (1.3)	44/50[b] (2.0)	50/50[b] (1.9)
Larynx				
Chronic inflammation	8/50 (1.8)	26/49[b] (1.5)	27/49[b] (1.3)	37/50[b] (1.4)
Degeneration of epiglottis respiratory epithelium	2/50 (1.0)	33/49[b] (1.2)	26/49[b] (1.2)	40/50[b] (1.5)
Hyperplasia of epiglottis respiratory epithelium	0/50	25/49[b] (1.4)	26/49[b] (1.3)	33/50[b] (1.5)
Squamous metaplasia of epiglottis respiratory epithelium	2/50 (2.0)	7/49 (1.9)	7/40 (1/7)	16/50[b] (1.4)
Nose				
Hyperplasia of respiratory epithelium goblet cell	13/50 (2.0)	18/50 (2.0)	16/50 (1.9)	30/50[b] (2.0)

[a]Average severity grade of lesions in affected animals: 1=minimal; 2=mild, 3=moderate; 4=marked
[b]$p \leq 0.01$
[c]$p \leq 0.05$

Source: NTP 2002

Dose and end point used for MRL derivation: The human equivalent concentration of the $BMCL_{10}$ for degeneration of respiratory epithelium of the epiglottis, 0.003 mg vanadium/m^3, was used as the point of departure for the chronic-duration inhalation MRL.

[ ] NOAEL [ ] LOAEL [X] $BMCL_{10}$

BMD analysis was used to determine the point of departure for select respiratory tract lesions in rats exposed to vanadium pentoxide for 2 years. A number of lesions were observed in male and female rats exposed to 0.28 mg vanadium/m^3 including hyperplasia of the alveolar and bronchiolar epithelium, chronic inflammation of the larynx, degeneration of the epiglottis, and hyperplasia of respiratory epithelial goblet cells. The incidence of these lesions in male rats were modeled using all available dichotomous models in the EPA BMDS (version 2.1) that were fit to the incidence data for alveolar hyperplasia, bronchial hyperplasia, using the extra risk option. The multistage model was run for all polynomial degrees up to n-1 (where n is the number of dose groups including control). Adequate model fit is judged by three criteria: goodness-of-fit p-value ($p>0.1$), visual inspection of the dose-response curve, and scaled residual at the data point (except the control) closest to the predefined BMR. Among all the models providing adequate fit to the data, the lowest BMCL is selected as the point of departure when the difference between the BMCLs estimated from these models are more three-fold; otherwise, the BMCL from the model with the lowest AIC is chosen. In accordance with U.S. EPA (2000) guidance, BMCs and BMCLs associated with an extra risk of 10% are calculated for all models.

The results of the BMD analyses are presented in Table A-3 and Figures A-2 through A-6.

Table A-3. Model Predictions for Respiratory Effects in Rats Exposed to Vanadium Pentoxide for 2 Years

Model	χ^2 Goodness of fit p-value[a]	AIC	BMC_{10} (mg V/m^3)	$BMCL_{10}$ (mg V/m^3)
Alveolar hyperplasia in male rats				
Gamma[b]	0.25	183.50	0.12	0.04
Logistic	0.52	181.44	0.11	0.09
Log-Logistic	0.08	185.40	NA	NA
Log-Probit	0.13	184.60	0.15	0.08
Multistage[c]	0.21	184.00	0.05	0.04
Probit	**0.57**	**181.29**	**0.10**	**0.09**
Weibull[b]	0.33	183.11	0.10	0.05
Quantal-Linear	0.21	184.00	0.05	0.04
Bronchiolar hyperplasia in male rats				
Gamma[b]	0.28	165.38	0.17	0.10
Logistic	0.60	163.19	0.15	0.12
Log-Logistic	0.08	167.58	NA	NA
Log-Probit	0.12	166.67	0.19	0.13
Multistage[c]	0.56	164.51	0.13	0.07
Probit	**0.71**	**162.87**	**0.14**	**0.12**
Weibull[b]	0.45	164.73	0.15	0.09
Quantal-linear	0.03	170.74		

Table A-3. Model Predictions for Respiratory Effects in Rats Exposed to Vanadium Pentoxide for 2 Years

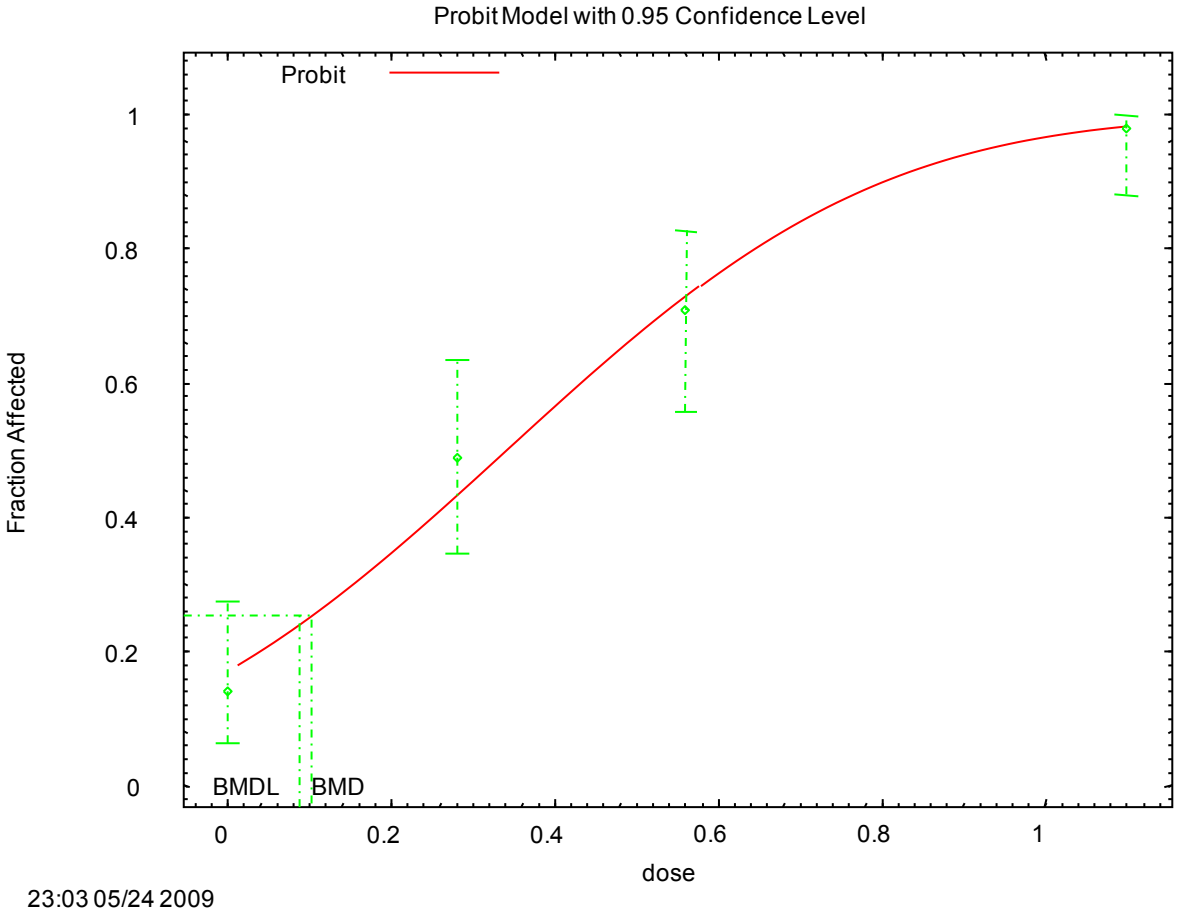
Model	χ^2 Goodness of fit p-value[a]	AIC	BMC_{10} (mg V/m^3)	$BMCL_{10}$ (mg V/m^3)
Chronic inflammation in larynx of male rats				
Gamma[b]	0.04	230.93	NA	NA
Logistic	0.01	235.47	NA	NA
Log-Logistic	**0.11**	**229.28**	**0.10**	**0.07**
Log-Probit	0.00	235.73	NA	NA
Multistage[c]	0.04	230.93	NA	NA
Probit	0.01	235.09	NA	NA
Weibull[b]	0.04	230.93	NA	NA
Quantal-linear	0.04	230.93	NA	NA
Degeneration of epiglottis respiratory epithelium in male rats				
Gamma[b]	0.06	210.55	NA	NA
Logistic	0.00	230.64	NA	NA
Log-Logistic	**0.47**	**206.17**	**0.06**	**0.04**
Log-Probit	0.01	214.79	NA	NA
Multistage[c]	0.06	210.55	NA	NA
Probit	0.00	229.81	NA	NA
Weibull[b]	0.06	210.55	NA	NA
Quantal-linear	0.06	210.55	NA	NA
Hyperplasia of nasal respiratory epithelial goblet cells in male rats				
Gamma[b]	0.12	213.84	0.32	0.20
Logistic	0.07	215.11	NA	NA
Log-Logistic	**0.15**	**213.35**	**0.27**	**0.16**
Log-Probit	0.03	216.79	NA	NA
Multistage[c]	0.12	213.84	0.32	0.20
Probit	0.07	214.97	NA	NA
Weibull[b]	0.12	213.84	0.32	0.20
Quantal-linear	0.12	213.84	0.32	0.20

[a]Values <0.10 fail to meet conventional goodness-of-fit criteria
[b]Power restricted to ≥1
[c]Betas restricted to ≥0; 1-degree polynomial

AIC = Akaike Information Criterion; BMD = maximum likelihood estimate of the dose/concentration associated with the selected benchmark response; BMDL = 95% lower confidence limit on the BMD; NA = not applicable

Source: NTP 2002

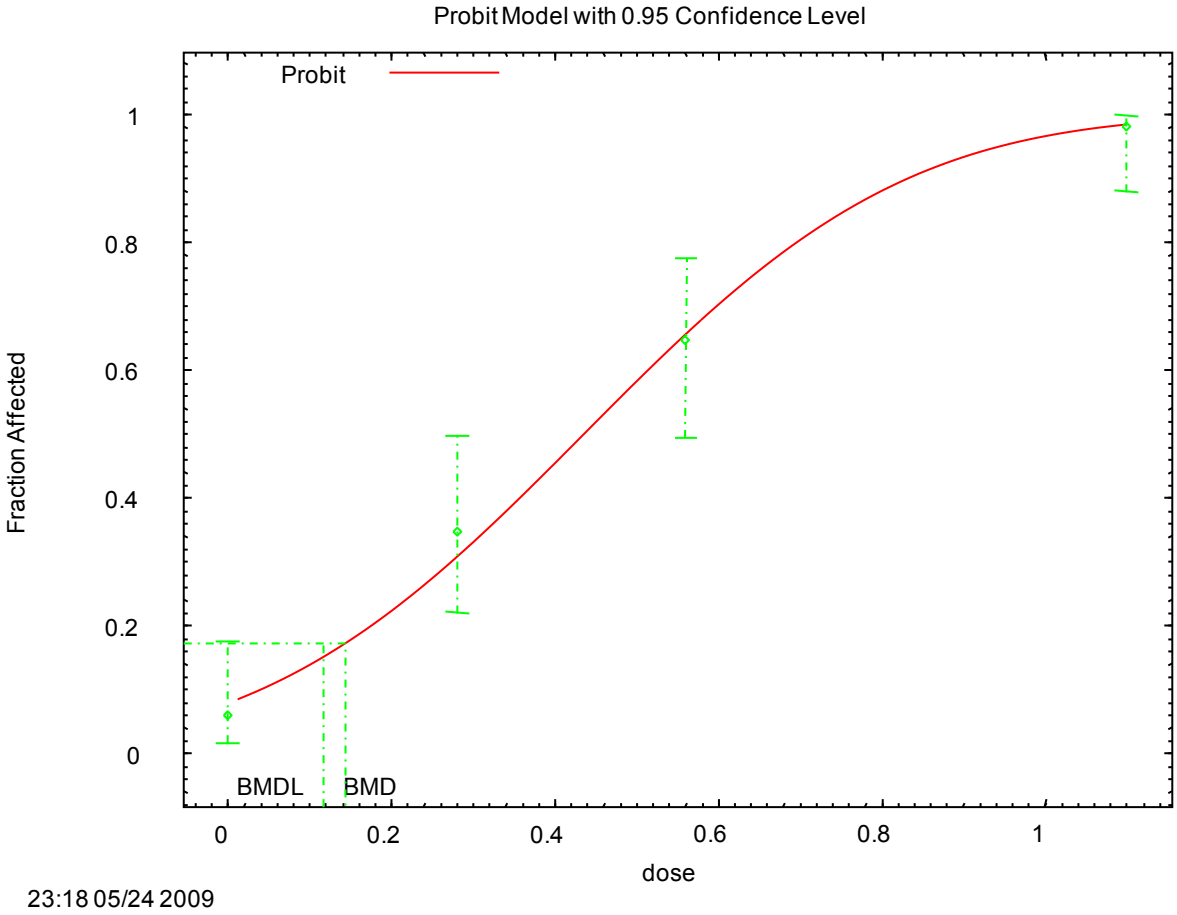
Figure A-2. Fit of Probit Model to Data on the Incidence of Alveolar Hyperplasia in Male Rats Exposed to Vanadium Pentoxide for 2 Years



BMCs and BMCLs indicated are associated with an extra risk of 10%, and are in units of mg vanadium/m^3

Source: NTP 2002

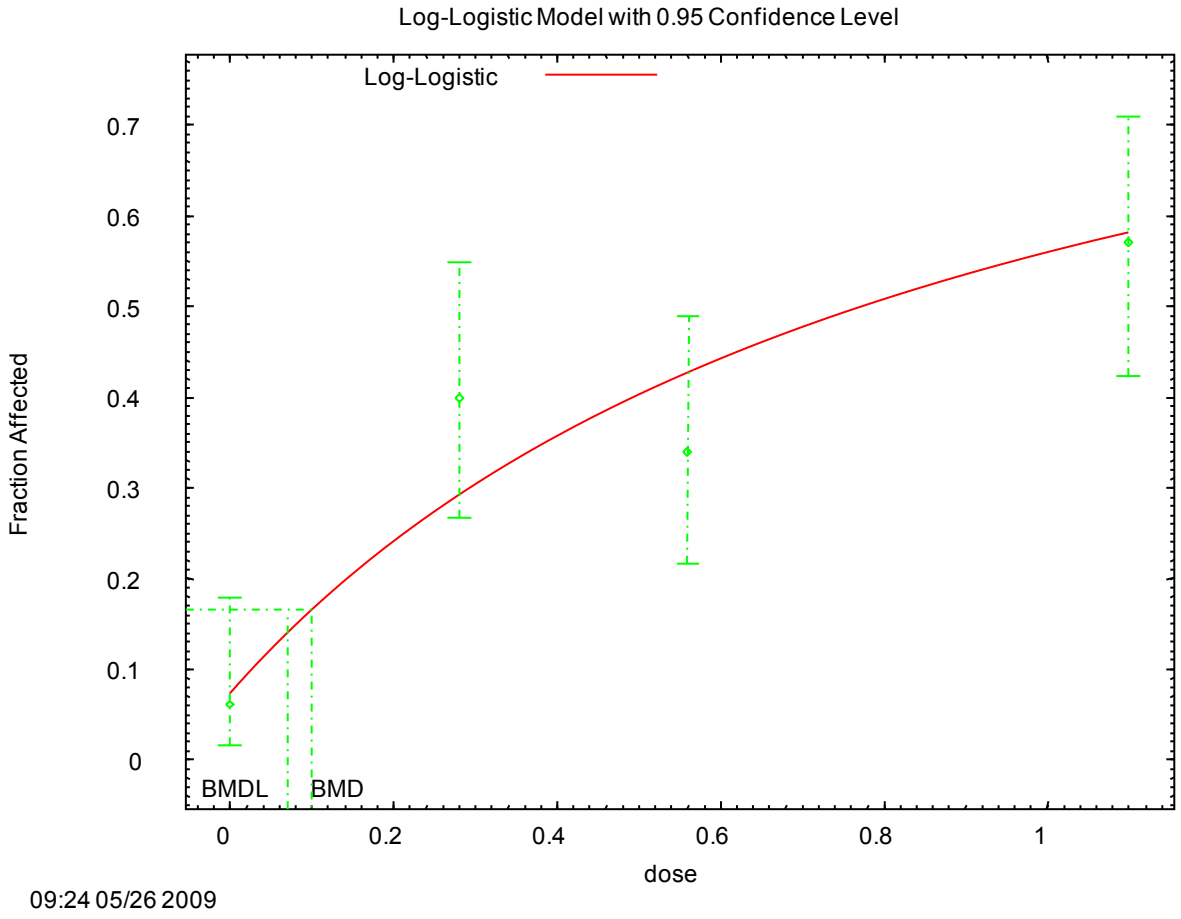
Figure A-3. Fit of Probit Model to Data on the Incidence of Bronchiolar Hyperplasia in Male Rats Exposed to Vanadium Pentoxide for 2 Years



BMCs and BMCLs indicated are associated with an extra risk of 10%, and are in units of mg vanadium/m^3

Source: NTP 2002

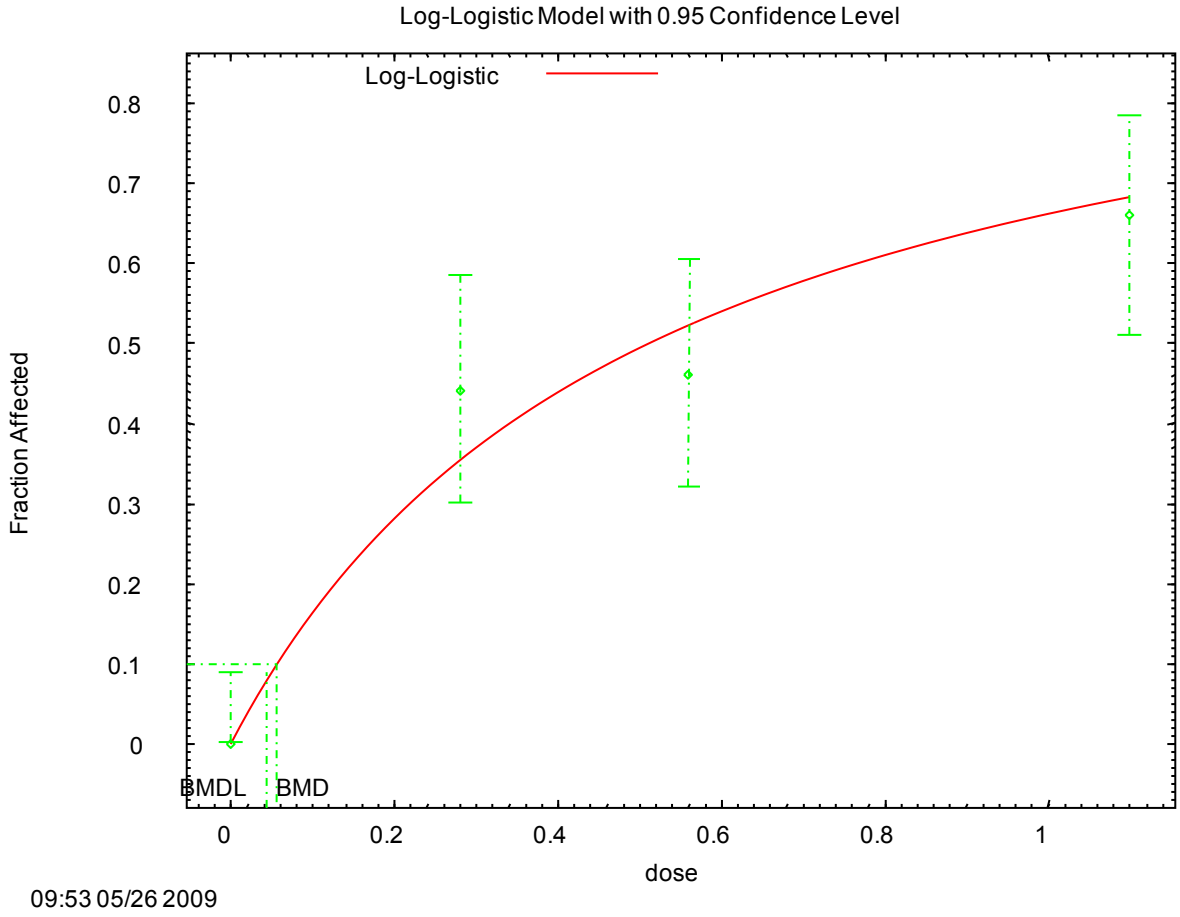
Figure A-4. Fit of Log-logistic Model to Data on the Incidence Chronic Inflammation in Larynx of Male Rats Exposed to Vanadium Pentoxide for 2 Years



BMCs and BMCLs indicated are associated with an extra risk of 10%, and are in units of mg vanadium/m^3

Source: NTP 2002

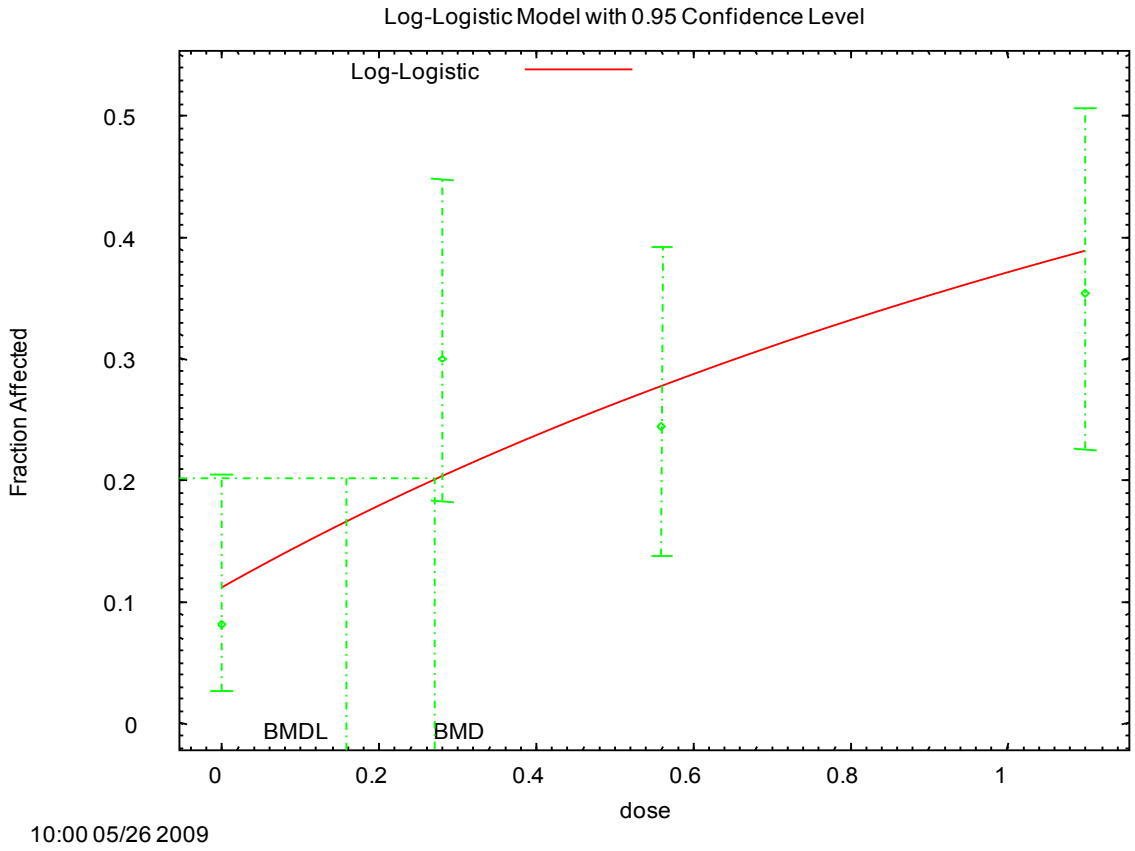
Figure A-5. Fit of Log-logistic Model to Data on the Incidence of Degeneration of Epiglottis Respiratory Epithelium in Male Rats Exposed to Vanadium Pentoxide for 2 Years



BMCs and BMCLs indicated are associated with an extra risk of 10%, and are in units of mg vanadium/m^3

Source: NTP 2002

Figure A-6. Fit of Log-logistic Model to Data on the Incidence of Hyperplasia of Nasal Respiratory Epithelial Goblet Cells in Male Rats Exposed to Vanadium Pentoxide for 2 Years



BMCs and BMCLs indicated are associated with an extra risk of 10%, and are in units of mg vanadium/m^3

Source: NTP 2002

In summary, the lowest $BMCL_{10}$ values for alveolar epithelial hyperplasia, bronchiolar epithelial hyperplasia, laryngeal chronic inflammation, degeneration of epiglottis epithelium, and hyperplasia of nasal goblet cells were 0.09, 0.10, 0.07, 0.04, 0.16 mg vanadium/m^3, respectively.

Uncertainty Factors used in MRL derivation:

[ ] 10 for use of a LOAEL
[X] 3 for extrapolation from animals to humans with dosimetric adjustments
[X] 10 for human variability

Was a conversion factor used from ppm in food or water to a mg/body weight dose? Not applicable.

If an inhalation study in animals, list conversion factors used in determining human equivalent dose:

Human equivalent concentrations were calculated for each $BMCL_{10}$ using the following equation:

$$BMCL_{HEC} = BMCL_{ADJ} \times RDDR$$

where:
The RDDR is a multiplicative factor used to adjust an observed inhalation particulate exposure concentration of an animal to the predicted inhalation particulate exposure concentration for a human. The RDDR program (EPA 1994c) was used to calculate a multiplier for the different regions of the respiratory tract was determined using a default body weight of 0.380 kg (EPA 1994c) and a particle size MMAD of 1.2 µm with a geometric standard deviation of 1.9. The $BMDL_{HEC}$ values are presented in Table A-4

Table A-4. Summary of Human Equivalent Concentrations of BMCL Values for Rats Exposed to Vanadium Pentoxide for 2 Years

Effect	$BMCL_{10}$ (mg vanadium/m^3)	$BMCL_{ADJ}$[a] (mg vanadium/m^3)	RDDR	$BMCL_{HEC}$ (mg vanadium/m^3)
Alveolar epithelial hyperplasia	0.09	0.016	0.502[b]	0.008
Bronchiolar epithelial hyperplasia	0.10	0.018	0.971[c]	0.017
Laryngeal chronic inflammation	0.07	0.012	0.423[d]	0.005
Degeneration of epiglottis epithelium	0.04	0.0071	0.423[d]	0.003
Hyperplasia of nasal goblet cells	0.16	0.029	0.423[d]	0.012

[a]$BMCL_{ADJ}$= $BMCL_{10}$ x 6 hours/24 hours x 5 days/7 days
[b]Pulmonary region
[c]Thoracic region
[d]Extrathoracic region

BMCL = benchmark concentration, lower confidence limit RDDR = regional deposited dose ratio

Source: NTP 2002

Was a conversion used from intermittent to continuous exposure? The $BMCL_{10}$ was adjusted for intermittent exposure, as noted in Table A-4.

Other additional studies or pertinent information that lend support to this MRL: An increased combined incidence of alveolar/bronchiolar adenoma or carcinoma was observed in male rats (NTP 2002). Although the incidence was not significantly higher than concurrent controls, it was higher than historical controls and NTP considered it to be a vanadium-related effect.

In mice exposed to ≥0.56 mg vanadium/m^3 for 6 hours/day, 5 days/week for 2 years, significant increases in the incidence of alveolar and bronchiolar hyperplasia, chronic lung inflammation, squamous metaplasia of the respiratory epithelium of the epiglottis, goblet cell hyperplasia in the nasal respiratory epithelium and nasal olfactory epithelial atrophy, and hyaline degeneration were observed (NTP 2002). In addition to these effects, a significant increase in alveolar/bronchiolar carcinoma incidence was also observed in mice exposed to ≥0.56 mg vanadium/m^3.

Agency Contacts (Chemical Managers): Jessilynn Taylor, Sam Keith, Larry Cseh

MINIMAL RISK LEVEL (MRL) WORKSHEET

Chemical Name: Vanadium compounds
CAS Numbers: 7440-62-6
Date: July 2012
Profile Status: Post-Public Comment, Third Draft
Route: [ ] Inhalation [X] Oral
Duration: [ ] Acute [X] Intermediate [ ] Chronic
Graph Key: 12
Species: Human

Minimal Risk Level: 0.01 [X] mg vanadium/kg/day [ ] mg vanadium/m^3

Reference: Fawcett JP, Farquhar SJ, Thou T, et al. 1997. Oral vanadyl sulphate does not affect blood cells, viscosity or biochemistry in humans. Pharmacol Toxicol 80:202-206.

Experimental design: Groups of men and women enrolled in a weight training program for at least 1 year were administered capsules containing 0 (11 men and 4 women) or 0.5 mg/kg/day vanadyl sulfate trihydrate (0.12 mg vanadium/kg/day) (12 men and 4 women) for 12 weeks. Fasting blood samples were collected at 0 and 12 weeks and analyzed for hematological (erthyroctye count, hemoglobin, hematocrit, mean cell volume, mean cell hemoglobin, platelet count, and total and differential leukocyte count) and serum chemistry (cholesterol, high density lipoprotein, triglycerides, albumin, total protein, total and direct bilirubin, alkaline phosphatase, ALT) parameters. Body weight and blood pressure were measured at weeks 4, 8, and 12.

Effect noted in study and corresponding doses: No significant alterations in blood pressure, body weight, or hematological or clinical chemistry parameters were found.

Dose and end point used for MRL derivation: NOAEL of 0.12 mg vanadium/kg/day for hematological alterations and blood pressure.

[X] NOAEL [ ] LOAEL

Uncertainty Factors used in MRL derivation:

[ ] 10 for use of a LOAEL
[ ] 10 for extrapolation from animals to humans
[X] 10 for human variability

Was a conversion factor used from ppm in food or water to a mg/body weight dose? No.

If an inhalation study in animals, list conversion factors used in determining human equivalent dose: Not applicable.

Was a conversion used from intermittent to continuous exposure? Not applicable.

Other additional studies or pertinent information that lend support to this MRL: Dimond et al. (1963) also examined healthy adults (one male and five females) administered an average daily dose of 0.19 mg vanadium/kg/day as ammonium vanadyl tartrate for 45–68 days and found no significant alterations in hematological or serum clinical chemistry parameters. Several studies have reported gastrointestinal effects in noninsulin-dependent diabetics that persisted for >2 weeks (Afkhami-Ardekani et al. 2008;

Goldfine et al. 2000). The signs of gastrointestinal irritation were likely due to local irritation rather than a systemic effect and were observed at 31.3 mg vanadium (administered 3 times/day); no effects were observed at 7.8 mg vanadium (Goldfine et al. 2000).

Studies in laboratory animals have identified several sensitive effects including alterations in erythrocyte and reticulocyte levels, increased blood pressure, neurobehavioral alterations, and developmental toxicity. Significant increases in blood pressure have been observed in rats exposed to 0.12 mg vanadium/kg/day for 210 days (Boscolo et al. 1994); increases in blood pressure have been observed at higher doses in several other studies by these investigators (Carmagnani et al. 1991, 1992). In general, other studies have not found increases in blood pressure in rats exposed to doses as high as 31 mg vanadium/kg/day (Bursztyn and Mekler 1993; Sušić and Kentera 1986, 1988). Decreases in erythrocyte levels have been observed in rats exposed to 1.18 mg vanadium/kg/day as ammonium metavanadate in drinking water for 4 weeks (Zaporowska et al. 1993); at higher concentrations, decreases in hemoglobin and increases in reticulocyte levels have been observed (Ścibior 2005; Ścibior et al. 2006; Zaporowska and Wasilewski 1990, 1991, 1992a, 1992b; Zaporowska et al. 1993). Decreases in pup body weight and length have been observed in the offspring of rats administered 2.1 mg vanadium/kg/day as sodium metavanadate for 14 days prior to mating and throughout gestation and lactation (Domingo et al. 1986). At higher doses (6, 10, or 12 mg vanadium/kg/day), decreases in pup survival, and increases in the occurrence of gross, visceral, or skeletal malformations and anomalies were observed (Elfant and Keen 1987; Morgan and El-Tawil 2003; Poggioli et al. 2001).

Agency Contacts (Chemical Managers): Jessilynn Taylor, Sam Keith, Larry Cseh

APPENDIX B. USER'S GUIDE

Chapter 1

Public Health Statement

This chapter of the profile is a health effects summary written in non-technical language. Its intended audience is the general public, especially people living in the vicinity of a hazardous waste site or chemical release. If the Public Health Statement were removed from the rest of the document, it would still communicate to the lay public essential information about the chemical.

The major headings in the Public Health Statement are useful to find specific topics of concern. The topics are written in a question and answer format. The answer to each question includes a sentence that will direct the reader to chapters in the profile that will provide more information on the given topic.

Chapter 2

Relevance to Public Health

This chapter provides a health effects summary based on evaluations of existing toxicologic, epidemiologic, and toxicokinetic information. This summary is designed to present interpretive, weight-of-evidence discussions for human health end points by addressing the following questions:

1. What effects are known to occur in humans?

2. What effects observed in animals are likely to be of concern to humans?

3. What exposure conditions are likely to be of concern to humans, especially around hazardous waste sites?

The chapter covers end points in the same order that they appear within the Discussion of Health Effects by Route of Exposure section, by route (inhalation, oral, and dermal) and within route by effect. Human data are presented first, then animal data. Both are organized by duration (acute, intermediate, chronic). *In vitro* data and data from parenteral routes (intramuscular, intravenous, subcutaneous, etc.) are also considered in this chapter.

The carcinogenic potential of the profiled substance is qualitatively evaluated, when appropriate, using existing toxicokinetic, genotoxic, and carcinogenic data. ATSDR does not currently assess cancer potency or perform cancer risk assessments. Minimal Risk Levels (MRLs) for noncancer end points (if derived) and the end points from which they were derived are indicated and discussed.

Limitations to existing scientific literature that prevent a satisfactory evaluation of the relevance to public health are identified in the Chapter 3 Data Needs section.

Interpretation of Minimal Risk Levels

Where sufficient toxicologic information is available, ATSDR has derived MRLs for inhalation and oral routes of entry at each duration of exposure (acute, intermediate, and chronic). These MRLs are not meant to support regulatory action, but to acquaint health professionals with exposure levels at which adverse health effects are not expected to occur in humans.

MRLs should help physicians and public health officials determine the safety of a community living near a chemical emission, given the concentration of a contaminant in air or the estimated daily dose in water. MRLs are based largely on toxicological studies in animals and on reports of human occupational exposure.

MRL users should be familiar with the toxicologic information on which the number is based. Chapter 2, "Relevance to Public Health," contains basic information known about the substance. Other sections such as Chapter 3 Section 3.9, "Interactions with Other Substances," and Section 3.10, "Populations that are Unusually Susceptible" provide important supplemental information.

MRL users should also understand the MRL derivation methodology. MRLs are derived using a modified version of the risk assessment methodology that the Environmental Protection Agency (EPA) provides (Barnes and Dourson 1988) to determine reference doses (RfDs) for lifetime exposure.

To derive an MRL, ATSDR generally selects the most sensitive end point which, in its best judgement, represents the most sensitive human health effect for a given exposure route and duration. ATSDR cannot make this judgement or derive an MRL unless information (quantitative or qualitative) is available for all potential systemic, neurological, and developmental effects. If this information and reliable quantitative data on the chosen end point are available, ATSDR derives an MRL using the most sensitive species (when information from multiple species is available) with the highest no-observed-adverse-effect level (NOAEL) that does not exceed any adverse effect levels. When a NOAEL is not available, a lowest-observed-adverse-effect level (LOAEL) can be used to derive an MRL, and an uncertainty factor (UF) of 10 must be employed. Additional uncertainty factors of 10 must be used both for human variability to protect sensitive subpopulations (people who are most susceptible to the health effects caused by the substance) and for interspecies variability (extrapolation from animals to humans). In deriving an MRL, these individual uncertainty factors are multiplied together. The product is then divided into the inhalation concentration or oral dosage selected from the study. Uncertainty factors used in developing a substance-specific MRL are provided in the footnotes of the levels of significant exposure (LSE) tables.

Chapter 3

Health Effects

Tables and Figures for Levels of Significant Exposure (LSE)

Tables and figures are used to summarize health effects and illustrate graphically levels of exposure associated with those effects. These levels cover health effects observed at increasing dose concentrations and durations, differences in response by species, MRLs to humans for noncancer end points, and EPA's estimated range associated with an upper- bound individual lifetime cancer risk of 1 in 10,000 to 1 in 10,000,000. Use the LSE tables and figures for a quick review of the health effects and to locate data for a specific exposure scenario. The LSE tables and figures should always be used in conjunction with the text. All entries in these tables and figures represent studies that provide reliable, quantitative estimates of NOAELs, LOAELs, or Cancer Effect Levels (CELs).

The legends presented below demonstrate the application of these tables and figures. Representative examples of LSE Table 3-1 and Figure 3-1 are shown. The numbers in the left column of the legends correspond to the numbers in the example table and figure.

LEGEND

See Sample LSE Table 3-1 (page B-6)

(1) Route of Exposure. One of the first considerations when reviewing the toxicity of a substance using these tables and figures should be the relevant and appropriate route of exposure. Typically when sufficient data exist, three LSE tables and two LSE figures are presented in the document. The three LSE tables present data on the three principal routes of exposure, i.e., inhalation, oral, and dermal (LSE Tables 3-1, 3-2, and 3-3, respectively). LSE figures are limited to the inhalation (LSE Figure 3-1) and oral (LSE Figure 3-2) routes. Not all substances will have data on each route of exposure and will not, therefore, have all five of the tables and figures.

(2) Exposure Period. Three exposure periods—acute (less than 15 days), intermediate (15–364 days), and chronic (365 days or more)—are presented within each relevant route of exposure. In this example, an inhalation study of intermediate exposure duration is reported. For quick reference to health effects occurring from a known length of exposure, locate the applicable exposure period within the LSE table and figure.

(3) Health Effect. The major categories of health effects included in LSE tables and figures are death, systemic, immunological, neurological, developmental, reproductive, and cancer. NOAELs and LOAELs can be reported in the tables and figures for all effects but cancer. Systemic effects are further defined in the "System" column of the LSE table (see key number 18).

(4) Key to Figure. Each key number in the LSE table links study information to one or more data points using the same key number in the corresponding LSE figure. In this example, the study represented by key number 18 has been used to derive a NOAEL and a Less Serious LOAEL (also see the two "18r" data points in sample Figure 3-1).

(5) Species. The test species, whether animal or human, are identified in this column. Chapter 2, "Relevance to Public Health," covers the relevance of animal data to human toxicity and Section 3.4, "Toxicokinetics," contains any available information on comparative toxicokinetics. Although NOAELs and LOAELs are species specific, the levels are extrapolated to equivalent human doses to derive an MRL.

(6) Exposure Frequency/Duration. The duration of the study and the weekly and daily exposure regimens are provided in this column. This permits comparison of NOAELs and LOAELs from different studies. In this case (key number 18), rats were exposed to “Chemical x” via inhalation for 6 hours/day, 5 days/week, for 13 weeks. For a more complete review of the dosing regimen, refer to the appropriate sections of the text or the original reference paper (i.e., Nitschke et al. 1981).

(7) System. This column further defines the systemic effects. These systems include respiratory, cardiovascular, gastrointestinal, hematological, musculoskeletal, hepatic, renal, and dermal/ocular. "Other" refers to any systemic effect (e.g., a decrease in body weight) not covered in these systems. In the example of key number 18, one systemic effect (respiratory) was investigated.

(8) NOAEL. A NOAEL is the highest exposure level at which no harmful effects were seen in the organ system studied. Key number 18 reports a NOAEL of 3 ppm for the respiratory system, which was used to derive an intermediate exposure, inhalation MRL of 0.005 ppm (see footnote "b").

(9) LOAEL. A LOAEL is the lowest dose used in the study that caused a harmful health effect. LOAELs have been classified into "Less Serious" and "Serious" effects. These distinctions help readers identify the levels of exposure at which adverse health effects first appear and the gradation of effects with increasing dose. A brief description of the specific end point used to quantify the adverse effect accompanies the LOAEL. The respiratory effect reported in key number 18 (hyperplasia) is a Less Serious LOAEL of 10 ppm. MRLs are not derived from Serious LOAELs.

(10) Reference. The complete reference citation is given in Chapter 9 of the profile.

(11) CEL. A CEL is the lowest exposure level associated with the onset of carcinogenesis in experimental or epidemiologic studies. CELs are always considered serious effects. The LSE tables and figures do not contain NOAELs for cancer, but the text may report doses not causing measurable cancer increases.

(12) Footnotes. Explanations of abbreviations or reference notes for data in the LSE tables are found in the footnotes. Footnote "b" indicates that the NOAEL of 3 ppm in key number 18 was used to derive an MRL of 0.005 ppm.

LEGEND

See Sample Figure 3-1 (page B-7)

LSE figures graphically illustrate the data presented in the corresponding LSE tables. Figures help the reader quickly compare health effects according to exposure concentrations for particular exposure periods.

(13) Exposure Period. The same exposure periods appear as in the LSE table. In this example, health effects observed within the acute and intermediate exposure periods are illustrated.

(14) Health Effect. These are the categories of health effects for which reliable quantitative data exists. The same health effects appear in the LSE table.

(15) Levels of Exposure. Concentrations or doses for each health effect in the LSE tables are graphically displayed in the LSE figures. Exposure concentration or dose is measured on the log scale "y" axis. Inhalation exposure is reported in mg/m^3 or ppm and oral exposure is reported in mg/kg/day.

(16) NOAEL. In this example, the open circle designated 18r identifies a NOAEL critical end point in the rat upon which an intermediate inhalation exposure MRL is based. The key number 18 corresponds to the entry in the LSE table. The dashed descending arrow indicates the extrapolation from the exposure level of 3 ppm (see entry 18 in the table) to the MRL of 0.005 ppm (see footnote "b" in the LSE table).

(17) CEL. Key number 38m is one of three studies for which CELs were derived. The diamond symbol refers to a CEL for the test species-mouse. The number 38 corresponds to the entry in the LSE table.

(18) Estimated Upper-Bound Human Cancer Risk Levels. This is the range associated with the upper-bound for lifetime cancer risk of 1 in 10,000 to 1 in 10,000,000. These risk levels are derived from the EPA's Human Health Assessment Group's upper-bound estimates of the slope of the cancer dose response curve at low dose levels (q_1*).

(19) Key to LSE Figure. The Key explains the abbreviations and symbols used in the figure.

SAMPLE

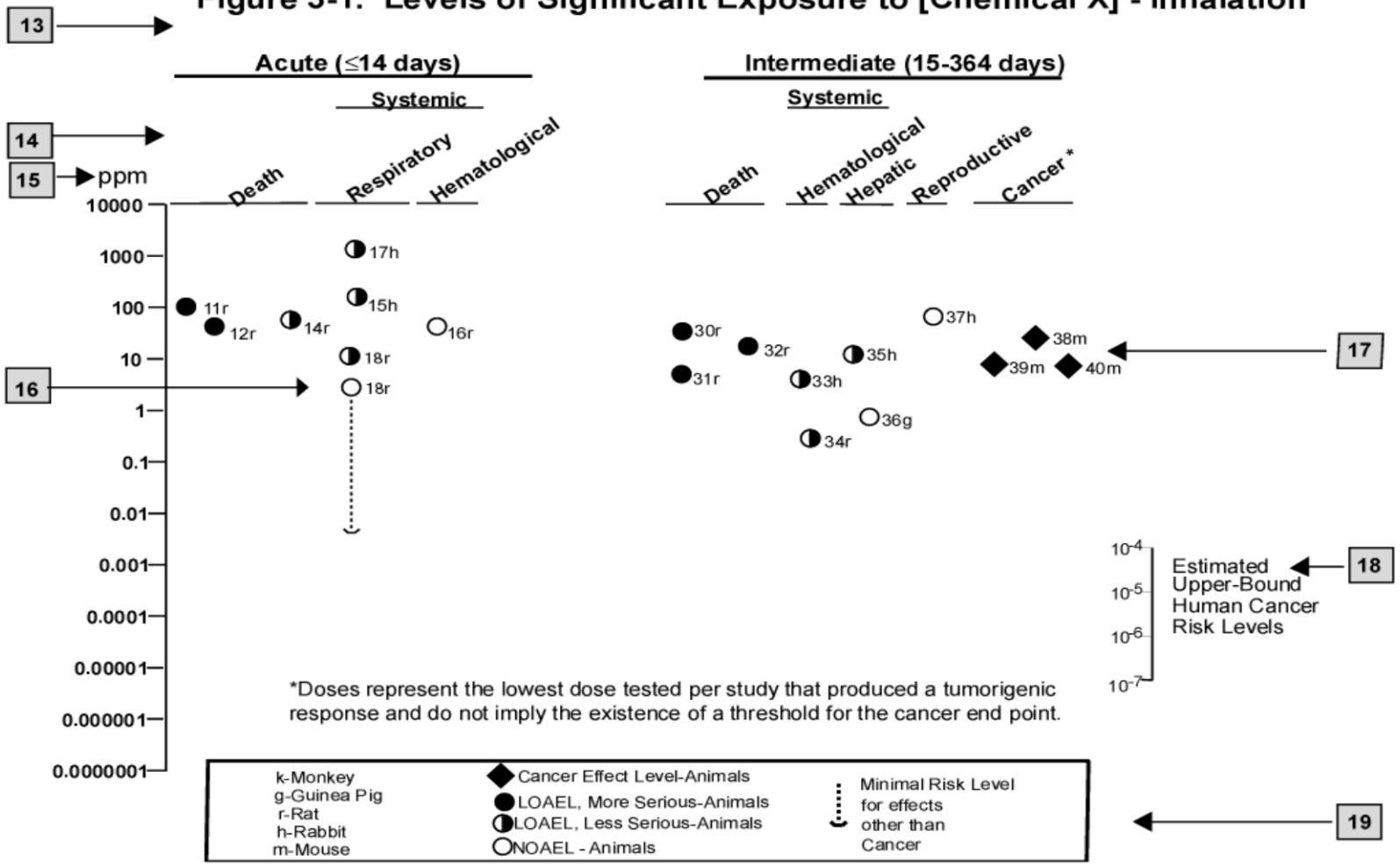
1 → **Table 3-1. Levels of Significant Exposure to [Chemical x] – Inhalation**

Key to figure[a]	Species	Exposure frequency/ duration	System	NOAEL (ppm)	LOAEL (effect) Less serious (ppm)	Serious (ppm)	Reference
2 → INTERMEDIATE EXPOSURE							
	5	6	7	8	9		10
3 → Systemic	↓	↓	↓	↓	↓		↓
18	Rat	13 wk 5 d/wk 6 hr/d	Resp	3[b]	10 (hyperplasia)		Nitschke et al. 1981
4 → CHRONIC EXPOSURE							
Cancer					11		
					↓		
38	Rat	18 mo 5 d/wk 7 hr/d			20	(CEL, multiple organs)	Wong et al. 1982
39	Rat	89–104 wk 5 d/wk 6 hr/d			10	(CEL, lung tumors, nasal tumors)	NTP 1982
40	Mouse	79–103 wk 5 d/wk 6 hr/d			10	(CEL, lung tumors, hemangiosarcomas)	NTP 1982

12 → [a] The number corresponds to entries in Figure 3-1.
[b] Used to derive an intermediate inhalation Minimal Risk Level (MRL) of $5x10^{-3}$ ppm; dose adjusted for intermittent exposure and divided by an uncertainty factor of 100 (10 for extrapolation from animal to humans, 10 for human variability).

SAMPLE

Figure 3-1. Levels of Significant Exposure to [Chemical X] - Inhalation



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APPENDIX C. ACRONYMS, ABBREVIATIONS, AND SYMBOLS

ACGIH	American Conference of Governmental Industrial Hygienists
ACOEM	American College of Occupational and Environmental Medicine
ADI	acceptable daily intake
ADME	absorption, distribution, metabolism, and excretion
AED	atomic emission detection
AFID	alkali flame ionization detector
AFOSH	Air Force Office of Safety and Health
ALT	alanine aminotransferase
AML	acute myeloid leukemia
AOAC	Association of Official Analytical Chemists
AOEC	Association of Occupational and Environmental Clinics
AP	alkaline phosphatase
APHA	American Public Health Association
AST	aspartate aminotransferase
atm	atmosphere
ATSDR	Agency for Toxic Substances and Disease Registry
AWQC	Ambient Water Quality Criteria
BAT	best available technology
BCF	bioconcentration factor
BEI	Biological Exposure Index
BMD/C	benchmark dose or benchmark concentration
BMD_X	dose that produces a X% change in response rate of an adverse effect
$BMDL_X$	95% lower confidence limit on the BMD_X
BMDS	Benchmark Dose Software
BMR	benchmark response
BSC	Board of Scientific Counselors
C	centigrade
CAA	Clean Air Act
CAG	Cancer Assessment Group of the U.S. Environmental Protection Agency
CAS	Chemical Abstract Services
CDC	Centers for Disease Control and Prevention
CEL	cancer effect level
CELDS	Computer-Environmental Legislative Data System
CERCLA	Comprehensive Environmental Response, Compensation, and Liability Act
CFR	Code of Federal Regulations
Ci	curie
CI	confidence interval
CL	ceiling limit value
CLP	Contract Laboratory Program
cm	centimeter
CML	chronic myeloid leukemia
CPSC	Consumer Products Safety Commission
CWA	Clean Water Act
DHEW	Department of Health, Education, and Welfare
DHHS	Department of Health and Human Services
DNA	deoxyribonucleic acid
DOD	Department of Defense
DOE	Department of Energy
DOL	Department of Labor

DOT	Department of Transportation
DOT/UN/ NA/IMDG	Department of Transportation/United Nations/ North America/Intergovernmental Maritime Dangerous Goods Code
DWEL	drinking water exposure level
ECD	electron capture detection
ECG/EKG	electrocardiogram
EEG	electroencephalogram
EEGL	Emergency Exposure Guidance Level
EPA	Environmental Protection Agency
F	Fahrenheit
F_1	first-filial generation
FAO	Food and Agricultural Organization of the United Nations
FDA	Food and Drug Administration
FEMA	Federal Emergency Management Agency
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FPD	flame photometric detection
fpm	feet per minute
FR	Federal Register
FSH	follicle stimulating hormone
g	gram
GC	gas chromatography
gd	gestational day
GLC	gas liquid chromatography
GPC	gel permeation chromatography
HPLC	high-performance liquid chromatography
HRGC	high resolution gas chromatography
HSDB	Hazardous Substance Data Bank
IARC	International Agency for Research on Cancer
IDLH	immediately dangerous to life and health
ILO	International Labor Organization
IRIS	Integrated Risk Information System
Kd	adsorption ratio
kg	kilogram
kkg	metric ton
K_{oc}	organic carbon partition coefficient
K_{ow}	octanol-water partition coefficient
L	liter
LC	liquid chromatography
LC_{50}	lethal concentration, 50% kill
LC_{Lo}	lethal concentration, low
LD_{50}	lethal dose, 50% kill
LD_{Lo}	lethal dose, low
LDH	lactic dehydrogenase
LH	luteinizing hormone
LOAEL	lowest-observed-adverse-effect level
LSE	Levels of Significant Exposure
LT_{50}	lethal time, 50% kill
m	meter
MA	*trans*,*trans*-muconic acid
MAL	maximum allowable level
mCi	millicurie

MCL	maximum contaminant level
MCLG	maximum contaminant level goal
MF	modifying factor
MFO	mixed function oxidase
mg	milligram
mL	milliliter
mm	millimeter
mmHg	millimeters of mercury
mmol	millimole
mppcf	millions of particles per cubic foot
MRL	Minimal Risk Level
MS	mass spectrometry
NAAQS	National Ambient Air Quality Standard
NAS	National Academy of Science
NATICH	National Air Toxics Information Clearinghouse
NATO	North Atlantic Treaty Organization
NCE	normochromatic erythrocytes
NCEH	National Center for Environmental Health
NCI	National Cancer Institute
ND	not detected
NFPA	National Fire Protection Association
ng	nanogram
NHANES	National Health and Nutrition Examination Survey
NIEHS	National Institute of Environmental Health Sciences
NIOSH	National Institute for Occupational Safety and Health
NIOSHTIC	NIOSH's Computerized Information Retrieval System
NLM	National Library of Medicine
nm	nanometer
nmol	nanomole
NOAEL	no-observed-adverse-effect level
NOES	National Occupational Exposure Survey
NOHS	National Occupational Hazard Survey
NPD	nitrogen phosphorus detection
NPDES	National Pollutant Discharge Elimination System
NPL	National Priorities List
NR	not reported
NRC	National Research Council
NS	not specified
NSPS	New Source Performance Standards
NTIS	National Technical Information Service
NTP	National Toxicology Program
ODW	Office of Drinking Water, EPA
OERR	Office of Emergency and Remedial Response, EPA
OHM/TADS	Oil and Hazardous Materials/Technical Assistance Data System
OPP	Office of Pesticide Programs, EPA
OPPT	Office of Pollution Prevention and Toxics, EPA
OPPTS	Office of Prevention, Pesticides and Toxic Substances, EPA
OR	odds ratio
OSHA	Occupational Safety and Health Administration
OSW	Office of Solid Waste, EPA
OTS	Office of Toxic Substances

OW	Office of Water
OWRS	Office of Water Regulations and Standards, EPA
PAH	polycyclic aromatic hydrocarbon
PBPD	physiologically based pharmacodynamic
PBPK	physiologically based pharmacokinetic
PCE	polychromatic erythrocytes
PEL	permissible exposure limit
pg	picogram
PHS	Public Health Service
PID	photo ionization detector
pmol	picomole
PMR	proportionate mortality ratio
ppb	parts per billion
ppm	parts per million
ppt	parts per trillion
PSNS	pretreatment standards for new sources
RBC	red blood cell
REL	recommended exposure level/limit
RfC	reference concentration
RfD	reference dose
RNA	ribonucleic acid
RQ	reportable quantity
RTECS	Registry of Toxic Effects of Chemical Substances
SARA	Superfund Amendments and Reauthorization Act
SCE	sister chromatid exchange
SGOT	serum glutamic oxaloacetic transaminase
SGPT	serum glutamic pyruvic transaminase
SIC	standard industrial classification
SIM	selected ion monitoring
SMCL	secondary maximum contaminant level
SMR	standardized mortality ratio
SNARL	suggested no adverse response level
SPEGL	Short-Term Public Emergency Guidance Level
STEL	short term exposure limit
STORET	Storage and Retrieval
TD_{50}	toxic dose, 50% specific toxic effect
TLV	threshold limit value
TOC	total organic carbon
TPQ	threshold planning quantity
TRI	Toxics Release Inventory
TSCA	Toxic Substances Control Act
TWA	time-weighted average
UF	uncertainty factor
U.S.	United States
USDA	United States Department of Agriculture
USGS	United States Geological Survey
VOC	volatile organic compound
WBC	white blood cell
WHO	World Health Organization

>	greater than
≥	greater than or equal to
=	equal to
<	less than
≤	less than or equal to
%	percent
α	alpha
β	beta
γ	gamma
δ	delta
μm	micrometer
μg	microgram
q_1^*	cancer slope factor
–	negative
+	positive
(+)	weakly positive result
(–)	weakly negative result

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APPENDIX D. INDEX