Appendix B

Comparison of Cal/EPA and US EPA Toxicity Values

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I. Introduction

At the meeting on dose-response assessment held at the University of California, Berkeley campus on November 15-16, 1995, the Risk Assessment Advisory Committee (Committee) requested California Environmental Protection Agency (Cal/EPA) to (1) identify chemicals whose toxicity values developed by Cal/EPA and US Environmental Protection Agency (US EPA) are significantly different and explain why, (2) identify chemicals that have a substantial impact on site-specific risk assessment results, and (3) explain the uncertainty factors used in the development of health-based drinking water guidance levels.

Cal/EPA prepared this document in response to the requests of the Committee. In Sections II and III, toxicity values used by Cal/EPA are compared to those used by US EPA. In general, Cal/EPA values are consistent with those shown in the US EPA Integrated Risk Information System (IRIS). However, for a small fraction of chemicals, Cal/EPA and US EPA toxicity values differ significantly (e.g., more than a factor of 5). Primary reasons for these differences are as follows:

- Toxicity values were derived at different time periods, typically with the more recent value reflecting methodological developments; the availability of more appropriate data; or greater consistency with standard risk assessment approaches.
- Different studies were selected as the basis of toxicity value development.
- Although the same study was selected by Cal/EPA and US EPA, the result was interpreted differently by the two agencies.

Section IV identifies the top 10 “risk drivers” in hazardous waste and the “Hot Spots” programs, indicates Cal/EPA and US EPA toxicity values, and describes the basis for these values. In Section V, the no-observed- or the lowest-observed-adverse health effects and the uncertainty factors used in the development of health-based drinking water standards are discussed.

It should also be noted that in the establishment of Cal/EPA in July1991, risk assessment programs from within the California Department of Health Services (CDHS) and the California Department of Food and Agriculture (CDFA) were moved to the new agency. Some of the values presented in this document were developed by these programs before 1991, and are currently used by Cal/EPA in its regulatory programs.

II. Comparison of Cal/EPA and US EPA Noncancer Toxicity Values

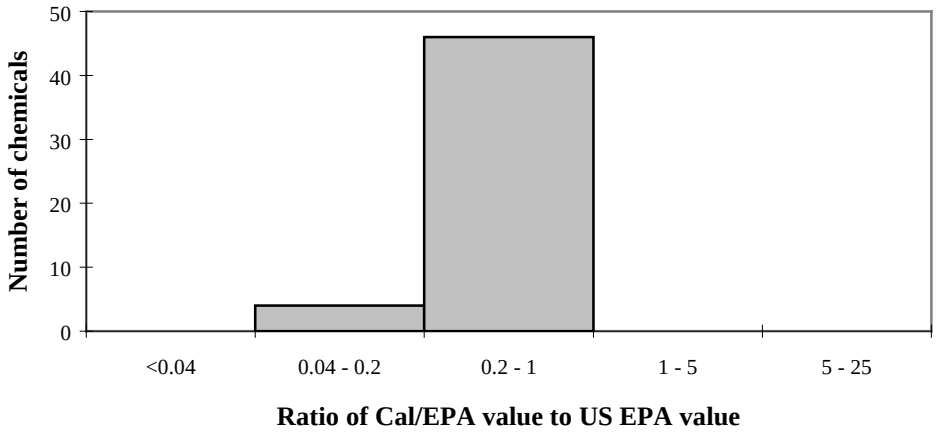
There are three sets of toxicity values maintained by Cal/EPA for the evaluation of chronic noncancer health effects. They are 1) the oral toxicity values developed and maintained by the Office of Environmental Health Hazard Assessment (OEHHA) for the

establishment of drinking water standards and action levels, 2) the chronic inhalation reference exposure levels (RELs) developed for the Air Toxics "Hot Spots" program, and 3) the No-Observed-Effect Levels (NOELs) of pesticides identified by Department of Pesticide Regulation (DPR) for the evaluation of pesticide tolerances and exposure levels. These three sets of toxicity values as well as those developed by US EPA, are included in Attachments B-1 through B-3 of this document. Also included are ratios of Cal/EPA to US EPA toxicity values; they are used in the identification of chemicals for which the Cal/EPA value differs significantly (by more than a factor of 5) from the US EPA number. Reasons for differences of this magnitude are discussed below.

A. Oral Toxicity Values for the Drinking Water Program

Cal/EPA has oral toxicity values for 61 chemicals. Of these, US EPA has toxicity values for 50. Based on the data shown in Attachment B-1, differences in oral toxicity values developed by Cal/EPA and US EPA are represented by the histogram shown below.

Comparison of Oral Toxicity Values Developed by Cal/EPA and US EPA for the Drinking Water Program



There are 4 compounds for which the Cal/EPA oral Reference Dose (RfD) value differs significantly (a factor of 5 or more) from the US EPA number. These 4 compounds are listed in the following table.

Substance	**Oral RfD (mg/kg-day)**	
	Cal/EPA	**US EPA**
cis-1,2-Dichloroethylene (cis-1,2-DCE)	0.00085	0.01
trans-1,2-Dichloroethylene (trans-1,2-DCE)	0.0017	0.017
1,1,2-Trichloro-1,2,2-trifluoroethane (Freon 113)	2.6	27
Xylenes (*o*-, *m*-, *p*-)	0.25	2

A brief description of the reasons for the difference is given below.

cis-1,2-Dichloroethylene (cis-1,2-DCE)

US EPA and Cal/EPA selected different studies for the development of the oral RfD. In the development of the Maximum Contaminant Level Goal (MCLG) for cis-1,2-DCE, US EPA (1991) used an oral 3-month study by McCauley et al. The agency's RfD workgroup reviewed the data and adopted an oral RfD of 0.01 mg/kg-day. The chronic noncancer toxicity value of this compound is currently under review by US EPA and the value has been removed from IRIS.

Cal/EPA's oral RfD for cis-1,2-DCE was developed in 1989 and is based on an earlier short-term inhalation study conducted by Freundt and Macholz (1978). The study by McCauley et al. was not available at that time. Based on the results of changes in hepatic xenobiotic metabolism in adult female Wistar rats, Cal/EPA identified a Lowest-Observed-Effect Level (LOEL) of 8.5 mg/kg-day. After applying an uncertainty factor of 10,000, to account for short-term animal data (10), interspecies extrapolation (10), sensitive individuals (10) and LOEL to NOEL extrapolation (10), Cal/EPA calculated an oral RfD of 0.00085 mg/kg-day for cis-1,2-DCE.

trans-1,2-Dichloroethylene (trans-1,2-DCE)

Both the US EPA and Cal/EPA values are based on the same 90-day mouse study in which trans-1,2-DCE was administered via drinking water (Barnes et al., 1985). The difference in assessments comes from a difference in interpretation of what constituted an adverse effect. US EPA (1991) defined the adverse effect as increased serum alkaline phosphatase levels which occurred at the higher dosages (175 and 387 mg/kg-day), but

was not apparent at the lowest dosage, 17 mg/kg-day. Thus, US EPA selected a NOEL of 17 mg/kg-day.

Cal/EPA (1989) noted that increases in serum glucose levels (apparent at the 17 mg/kg-day dosage) in conjunction with decreases in liver enzyme activity (namely, serum glutamic-pyruvic transaminase and serum glutamic-oxaloacetic aniline hydroxylase) observed at all dosages were indicative of hepatic dysfunction. Thus, Cal/EPA defined the lowest dosage, 17 mg/kg-day, as the LOEL. Cal/EPA subsequently divided the toxicity estimate by an additional 10-fold uncertainty/adjustment factor to account for using a LOEL instead of a NOEL.

1,1,2-Trichloro-1,2,2-trifluoroethane (Freon 113)

US EPA and Cal/EPA selected different studies for the development of oral RfDs for Freon 113. In 1990, US EPA revised the toxicity value of this compound on IRIS. The result from an epidemiological study where workers were exposed to airborne Freon 113 (Imbus and Adkins, 1972) was used to develop the new guidance toxicity value. The NOEL reported in this study was 5358 mg/m^3, which can be converted to 273 mg/kg-day assuming an inhalation rate of 10 m^3/8-hr, an exposure frequency of 5 days/week, an absorption efficiency of 0.5, and a body weight of 70 kg. In order to account for human inter-individual variability, US EPA applied an adjustment factor of 10 to the NOEL to reach an oral RfD of 27 mg/kg-day. However, US EPA has not used this RfD to develop a federal MCLG for Freon 113 in drinking water.

Cal/EPA (1989) used a two-year chronic toxicity study conducted in rats (du Pont, 1985) to identify the LOEL for Freon 113. In this study, groups of 100 male and female Crl:CDR (SD) BR rats were exposed to 0, 2,000, 10,000 or 19,900 ppm of Freon 113 vapor 5 days a week, 6 hours per day over a two-year period. The researchers reported a statistically significant increase in relative liver weights for male rats in all exposure groups. Based on this information, Cal/EPA identified 2,000 ppm as the LOEL. Using 0.65 l/min/kg as the rat respiratory minute volume, 360 min as the total daily exposure duration and 100% absorption efficiency assumption, this corresponds to a LOEL of 2574 mg/kg-day. After applying an uncertainty/adjustment factor of 100 to account for LOEL to NOEL as well as species-to-species extrapolation, and a factor of 10 for inter-individual variability, Cal/EPA calculated an oral RfD of 2.6 mg/kg-day.

Xylenes (*o-, m-, p-*)

Both US EPA and Cal/EPA used the same National Toxicology Program (NTP) rat study (1986) for the determination of an oral RfD for xylene. In the study, groups of 50 male and female Fischer 344 rats were given gavage doses of 0, 250, or 500 mg/kg-day of mixed xylene (60.2 % m-xylene, 13.6 % p-xylene, 17.0 % ethylbenzene and 9.1 % o-xylene) for 5 days/week for 103 weeks. US EPA (1991) identified no adverse effect in the low dose group and after adjusting for exposure frequency estimated a NOEL of 179 mg/kg-day. US EPA subsequently divided the toxicity estimate by an uncertainty factor of 100 to arrive at an oral RfD of 1.79 mg/kg-day which can be rounded to 2 mg/kg-day.

The uncertainty factor includes a factor of 10 for species-to-species extrapolation and another factor of 10 to protect sensitive individuals.

Cal/EPA (1989) reviewed the same study and identified 250 mg/kg-day as the LOEL. This is because the mean body weights of male rats dosed with 250 mg/kg-day of mixed xylene isomers tended to be lower than those of vehicle control male rats especially after 90 weeks. Cal/EPA then applied an uncertainty factor of 100 for extrapolating from long-term animal data to human exposure and an additional factor of 10 for using LOEL instead of NOEL. Thus, Cal/EPA calculated an oral RfD of 0.25 mg/kg-day for mixed xylene isomers, and this is the reason for the 8-fold difference in the State of California's and US EPA's toxicity estimate.

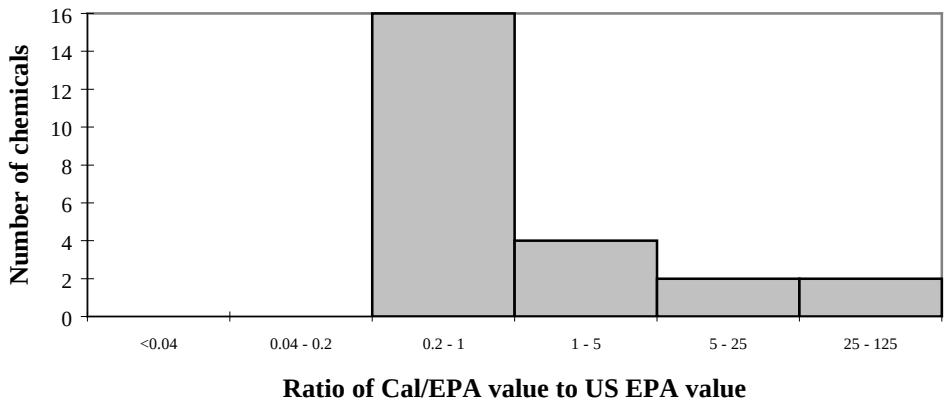
B. Chronic Inhalation Toxicity Values for the Air Toxics "Hot Spots" Program

The chronic inhalation toxicity values in the Air Toxics "Hot Spots" Program were initially developed by CAPCOA in consultation with OEHHA. The CAPCOA values largely reflect preliminary methodologies available early in the "Hot Spots" program's history. New guidelines are being developed and are expected to be available for public review and comment by the end of 1996.

In the development of these guidelines, US EPA Reference Concentrations (RfCs) are being assessed on a case-by-case basis to determine if the RfC still reflects the best available information and is, therefore, appropriate for adoption.

Under the Air Toxics "Hot Spots" Program, Cal/EPA has developed chronic inhalation toxicity values for 94 chemicals. Of these there are 24 for which US EPA has toxicity values. Based on the data shown in Attachment B-2, differences in chronic inhalation values developed by Cal/EPA and US EPA are represented by the histogram shown below.

Comparison of Chronic Inhalation Toxicity Values Developed by Cal/EPA and US EPA



There are 4 compounds for which the CAPCOA value differs by a factor of 5 or more from the US EPA number.

Substance	Chronic Inhalation Toxicity Value ($\mu g/m^3$)		
	Cal/EPA, REL[a]		US EPA, RfC
Hydrogen cyanide	70	{IRIS}	3
Hydrogen sulfide	42	CAAQS	1
Manganese	0.4	IRIS	0.05
Phosphine	10	{IRIS}	0.3

[a] Origin of CAPCOA value: {IRIS} indicates values derived from adjusting a US EPA IRIS oral value; CAAQS indicates the California Ambient Air Quality Standard (1 hour for hydrogen sulfide)

A brief description of the reasons for the difference are noted below.

Hydrogen cyanide

CAPCOA did not derive an original value for a non-cancer chronic REL. The REL for hydrogen cyanide was derived by adjusting the IRIS oral RfD to an equivalent inhalation value for a 70 kg person breathing 20 m^3/day. At the time the REL for hydrogen cyanide was developed, the US EPA RfC value of 3 $\mu g/m^3$ was not available. The US EPA RfC appears to be more appropriate because it uses inhalation data.

Hydrogen sulfide

CAPCOA did not derive an original value for a non-cancer chronic REL. CAPCOA adopted the one-hour California Ambient Air Quality Standard (CAAQS) of 42 µg/m^3. At the time the REL for hydrogen sulfide was developed, the US EPA RfC of 1 µg/m^3 was not available. The US EPA RfC appears to be more appropriate since the CAAQS is based on odor perception rather than adverse health effects.

Manganese

CAPCOA did not derive an original value for a non-cancer chronic REL. CAPCOA adopted the older US EPA RfC of 0.4 µg/m^3. The more recent US EPA RfC of 0.05 µg/m^3 appears to be more appropriate.

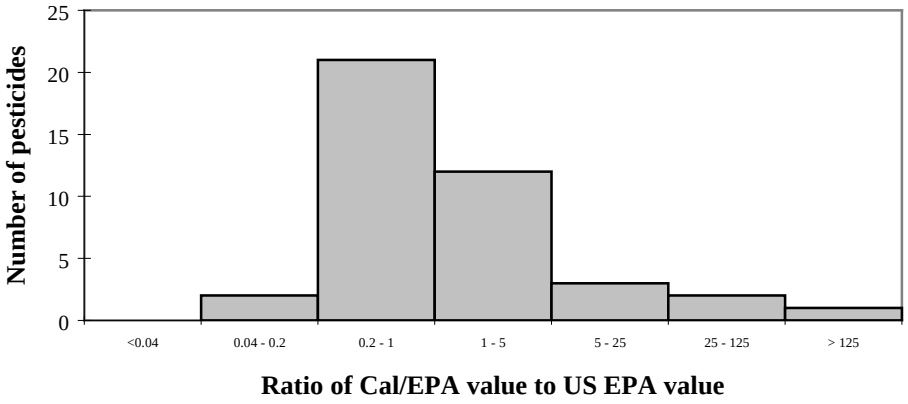
Phosphine

CAPCOA did not derive an original value for a non-cancer chronic REL. The CAPCOA REL of 10 µg/m^3 was derived by adjusting the US EPA oral RfD of 0.3 µg/kg/day to an equivalent inhalation concentration for a 70 kg person breathing 20 m^3/day. The US EPA RfC of 0.3 µg/m^3 uses inhalation data and therefore appears to be more appropriate. The US EPA RfC value was not available when CAPCOA adopted its value.

C. DPR Pesticide Program

Based on the comparison of chronic NOELs developed by Cal/EPA and US EPA shown in Attachment B-3, a histogram is prepared to show the distribution of differences in NOELs developed by Cal/EPA and US EPA.

Comparison of Chronic NOELs Developed by Cal/EPA and US EPA for Pesticides



There are 10 compounds for which the Cal/EPA chronic NOEL is different by at least 5-fold from the US EPA number; they are listed in the table below.

Substance	**NOEL (mg/kg-day)**	
	Cal/EPA, DPR [a]	**US EPA [b]**
Captafol [c]	2.9	(0.2) [d]
Chlorpyrifos	1.0	0.03
EPTC	0.5	2.5
Ethyl parathion [e]	0.4	(0.001) [d]
Fenamiphos	0.5	0.01
Isofenphos	0.5	0.05
Molinate	1	0.2
Monocrotophos [f]	0.05	0.0045
Tralomethrin	(0.075) [d]	0.75
Triadimefon	2.5	11.4

a These values represent the current status and could be revised with the consideration of additional data. With the exception of isofenphos, Cal/EPA, DPR selected different studies for NOEL determination.
b Obtained from RfD tracking report (US EPA, OPP, September, 1995)
c Captafol is no longer registered in California or federally since 1988 making evaluation of differences difficult.
d Estimated from LOEL values using an uncertainty factor of 10.
e Ethyl parathion is no longer registered in California or federally since 1992.
f Monocrotophos is no longer registered in California or federally since 1989.

A brief description of the reasons for the difference are noted below. In all cases except for isofenphos, DPR's toxicity guidance value is selected from a different study from US EPA's value.

Chlorpyrifos

US EPA (latest review: 1995) established a critical chronic NOEL at 0.03 mg/kg-day based on the inhibition of plasma cholinesterase in a 20-day human study. DPR does not consider the endpoint (plasma cholinesterase inhibition) a toxicologically significant effect. In the absence of cholinergic signs and/or brain cholinesterase inhibition, DPR does not consider plasma or erythrocyte cholinesterase inhibition per se as a toxicologically significant effect on which to establish a critical NOEL, and also 20 days is not generally sufficient to constitute chronic exposure. Therefore, DPR did not use this study to establish a critical chronic NOEL.

DPR (1992) established the critical chronic NOEL at 1 mg/kg-day based on the inhibition of brain cholinesterase at one-year in dog and rat feeding studies. DPR used 1 mg/kg-day as the NOEL to assess chronic dietary, residential and occupational exposures.

EPTC (Dipropylcarbamothioic Acid S-Ethyl Ester or Dipropylthiocarbamic Acid S-Ethyl Ester)

US EPA (latest review: 1987) established a critical chronic NOEL of 2.5 mg/kg-day based on degenerative cardiomyopathy in a rat reproduction study.

DPR (1993 draft) established a critical chronic NOEL (estimated) of 0.5 mg/kg-day based on neuromuscular degeneration in a two-year rat feeding study. This effect was present at all doses including the lowest dose of 5 mg/kg-day; therefore, DPR, using a default procedure of dividing the LOEL by 10, calculated an estimated NOEL of 0.5 mg/kg-day to assess chronic exposures.

Ethyl Parathion

US EPA (latest review : 1986) established the LOEL of 0.01 mg/kg-day in a one-year feeding study in dogs based on the inhibition of plasma and erythrocyte cholinesterase. Using a default uncertainty factor of 10, the estimated NOEL was 0.001 mg/kg-day.

DPR (1992) established the chronic NOEL of 0.4 mg/kg-day in a two-year feeding study in rats based on ocular effects, tremors, and body weight reduction observed at 1.6 mg/kg-day. DPR used 0.4 mg/kg-day as the NOEL to assess chronic ambient air exposures.

Fenamiphos

US EPA (latest review: 1993) established a critical chronic NOEL of 0.01 mg/kg-day (0.5 ppm) based on the inhibition of plasma cholinesterase activity in a one-year dog feeding study. DPR established NOELs of 0.03 mg/kg-day and 0.09 mg/kg-day for the inhibition of plasma and brain cholinesterase, respectively, in the same dog study.

DPR (1992) established a critical chronic NOEL of 0.5 mg/kg-day in a two-year rat feeding study based on systemic toxicity (inflammatory lesions of the nasal, laryngeal and lung tissues) and brain cholinesterase inhibition. DPR used the NOEL to assess chronic dietary exposures.

Isofenphos

US EPA (latest review: 1994) established the critical chronic NOEL at 0.05 mg/kg-day (1 ppm) based on erythrocyte cholinesterase inhibition in a two-year rat feeding study.

In the review of the same rat feeding study, DPR (1991) concurred with US EPA in establishing the NOEL for erythrocyte cholinesterase inhibition at 1 ppm. However, in the absence of cholinergic signs or symptoms at 0.5 mg/kg-day, the critical NOEL was established at 0.5 mg/kg-day (10 ppm) based on cholinergic signs at the next higher dose of 5 mg/kg-day. This NOEL was used to assess chronic exposures.

Molinate

US EPA (latest review: 1988) established a critical chronic NOEL of 0.2 mg/kg-day based on sperm abnormalities in a 30-day rat study conducted in 1981. Since the use of molinate as a rice herbicide is truly seasonal, DPR established a seasonal NOEL of 0.48 mg/kg-day based on sperm abnormalities in a subchronic rat study submitted to DPR in 1993.

DPR (1995 draft) established a critical chronic NOEL at 1 mg/kg-day based on neurotoxicity in a one-year dog feeding study. DPR used 1 mg/kg-day as the NOEL to assess chronic exposure and 0.48 mg/kg-day as the NOEL to assess seasonal exposure.

Monocrotophos_
(Note: US EPA canceled the federal registration of monocrotophos in 1989.)

US EPA (latest review: 1986) established a critical chronic NOEL of 0.0045 based on decreased plasma, erythrocyte and brain cholinesterase activities in a two-year rat feeding study.

DPR (1989) established a critical chronic NOEL of 0.05 mg/kg-day based increased pre-weaning loss and poor mammary gland development in a rat reproduction study. DPR used this NOEL to assess chronic occupational exposures.

Tralomethrin

US EPA (latest review: 1989) established the critical chronic NOEL of 0.75 mg/kg-day in a two-year rat feeding study based on decreased body weight in males, increased food and water consumption in males and females at 3 mg/kg-day.

In the two-year rat feeding study, DPR (1995) considered the NOEL to be 3 mg/kg-day based on excessive salivation, uncoordinated movements, and an inability to support weight on limbs at 12 mg/kg-day. In a two-year feeding study with mice, DPR established a LOEL at 0.75 mg/kg-day, the lowest dose tested, based on chronic dermatitis. DPR calculated an estimated NOEL of 0.075 mg/kg-day by using the default

procedure of dividing the LOEL by an uncertainty factor of 10. This NOEL is used by DPR to assess chronic dietary and occupational exposures.

Triadimefon

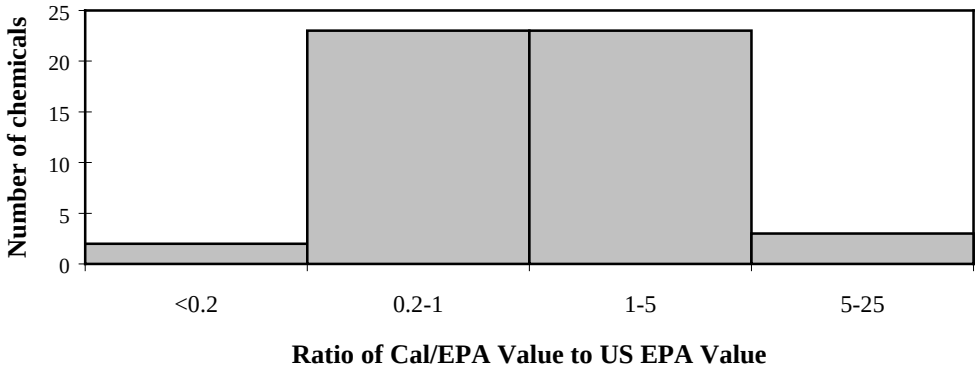
US EPA initially (1986) established a critical chronic NOEL of 2.5 mg/kg-day (50 ppm) based on decreased body weight, decreased hematological parameters in a two-year rat feeding study. In 1995, US EPA changed the critical chronic NOEL and subsequent RfD to 11.4 mg/kg-day (330 ppm) and 0.04 mg/kg-day, respectively. The NOEL was based on decreased food intake, decreased weight gain and changes in various clinical chemistry parameters in a two-year dog feeding study. An uncertainty factor of 300 was used in establishing the RfD.

DPR has reviewed (1985, 1992) the two-year dog study and agrees with US EPA that the NOEL for this study is 330 ppm; however, DPR decided to use the NOEL of 2.5 mg/kg-day from the two-year rat study to assess chronic exposure, primarily because the endpoints in the dog study are not considered as more "adverse" than the endpoints in the rat study and the NOEL for the rat study is lower than the NOEL in the dog study. DPR used this NOEL to assess chronic exposures.

III. Comparison of Cal/EPA and US EPA Cancer Potency Values

Cal/EPA has consensus oral potency values for 210 compounds. Among this group of chemicals, US EPA currently lists 52 oral potency values in IRIS (US EPA, 1996), the agency's official repository of agency-wide consensus health risk information. The US EPA 1995 *Health Effects Assessment Summary Tables* (HEAST) provides an additional 19 "provisional" oral potency values. US EPA notes that provisional values have not "had enough review to be recognized as high quality agency-wide consensus information". For comparison purpose, only ratios of the Cal/EPA and US EPA consensus values were calculated. The results of this analysis are presented below as a histogram. Attachment B-4 displays the oral cancer potency values used by Cal/EPA and listed in US EPA's IRIS and HEAST.

Comparison of Cal/EPA and US EPA Oral Cancer Potency Values for Carcinogens



For 5 (10%) of these compounds, the oral cancer potency values for the two agencies differ by a factor of 5 or more (see table below). The reasons why the Cal/EPA and US EPA numbers differ for these 5 agents are discussed below.

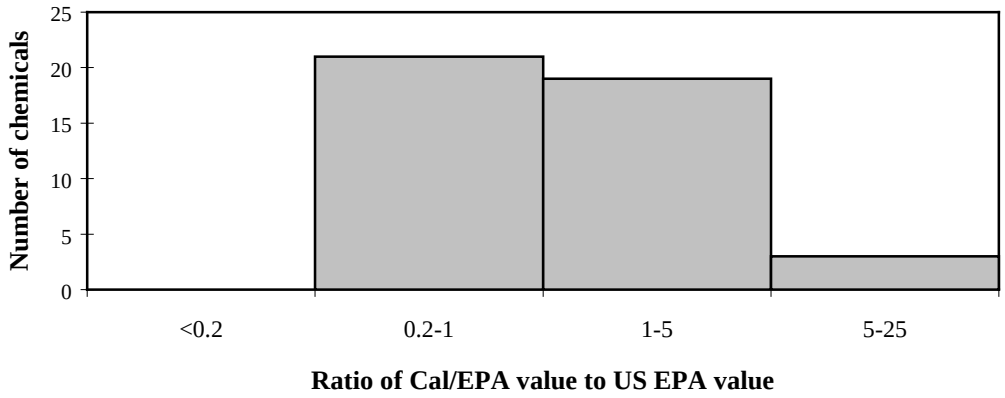
Cal/EPA and US EPA Oral Cancer Potency Values that Differ by a Factor of 5 or More

Chemical	Oral Cancer Potency $(mg/kg\text{-}day)^{-1}$	
	Cal/EPA	US EPA
Chloroform	0.031	0.0061
1,2-Dibromoethane	3.6	85
Epichlorohydrin	0.08	0.0099
Pentachlorophenol	0.018[a]	0.12
2,4,6-Trichlorophenol	0.07	0.011

[a]A value of 0.158 $[mg/kg\text{-}day]^{-1}$ has been proposed in the draft Cal/EPA OEHHA (1994) *Recommended Public Health Level for Pentachlorophenol in Drinking Water*.

Cal/EPA has consensus inhalation unit risk values for 215 compounds. Among this group of chemicals, US EPA currently lists 44 inhalation unit risk factors in IRIS (US EPA, 1996), the agency's official repository of agency-wide consensus health risk information. The US EPA 1995 HEAST provides an additional 5 "provisional" inhalation unit risk factors. US EPA notes that provisional values have not "had enough review to be recognized as high quality agency-wide consensus information". For comparison purpose, only ratios of the Cal/EPA and US EPA consensus values were calculated. The results of this analysis are presented below as a histogram. Attachment B-4 displays the inhalation unit risk factors used by Cal/EPA and listed in US EPA's IRIS and HEAST.

Comparison of Cal/EPA and US EPA Inhalation Unit Risk Values for Carcinogens



The inhalation unit risk values for the two agencies differ by a factor of 5 or more for only 3 agents (7%) (see Table below). The reasons why the Cal/EPA and US EPA numbers differ for these 3 agents are discussed below.

Cal/EPA and US EPA Inhalation Unit Risk Values that Differ by a Factor of 5 or More

Chemical	Inhalation Unit Risk $(\mu g/m^3)^{-1}$	
	Cal/EPA	US EPA
Chromium (VI)	1.5×10^{-1}	1.2×10^{-2}
Epichlorohydrin	2.3×10^{-5}	1.2×10^{-6}
2,4,6-Trichlorophenol	2.0×10^{-5}	3.1×10^{-6}

Chloroform

The inhalation unit risk values derived by Cal/EPA and US EPA differ by a factor of 4.3 and estimates of cancer potencies for oral exposure by these two agencies differ by a factor of 5.1. Differences between the Cal/EPA and US EPA values are primarily due to the selection of bioassay data sets on which to base the potency estimates.

The US EPA oral cancer potency (0.0061 $[mg/kg\text{-}day]^{-1}$) was derived by applying the linearized multistage procedure to the kidney tumors data from the drinking water study in male Osborne Mendel rats reported by Jorgensen et al. (1985). The US EPA inhalation unit risk was derived from dose-response data for liver carcinoma in the gavage study in female mice reported by the National Cancer Institute (NCI, 1976). Latest US EPA review of the inhalation and oral values on US EPA IRIS was conducted in 1987.

The Cal/EPA oral value (0.031 [mg/kg-day]$^{-1}$) was derived in 1990. Cancer potency estimates were derived from several oral studies and included consideration of dose-dependent pharmacokinetics through a PBPK ("physiologically-based phamacokinetic") model. The best estimate is a weighted average of 13 cancer potency estimates corresponding to 13 different oral experiments in mice and rats. The results for the liver tumors in mice observed in the NCI corn oil gavage study were excluded due to the possibility that the production of the tumors was vehicle dependent. Potencies derived from the male rat kidney tumors reported by Jorgensen et al. and by the NCI were weighted most heavily because these were judged to be the more reliable results for potency estimation. The Cal/EPA inhalation value (0.019 [mg/kg-day]$^{-1}$, or 5.3×10^{-6} [μg/m^3]$^{-1}$) was derived in the same fashion after taking into account differences in pharmacokinetics between the oral and inhalation route.

Chromium (hexavalent)

The primary concern in site-specific risk assessments is cancer from inhalation exposure to hexavalent chromium. The US EPA and Cal/EPA inhalation unit risks differ by a factor of 12.5. The CDHS (1985) value and US EPA (1984) value were both based on the dose response for lung cancer in chromate production workers, as reported by Mancuso (1975).

In deriving the unit risk value, US EPA (1984) took into consideration that one-seventh (14%) of the total chrome was hexavalent chromium, that 1949 industrial hygiene data may have underestimated exposures, and that chromate workers were likely to have had a higher smoking rate than white males in the general population. Because the first factor could lead to an underestimation (approximately 7-fold) of risk and the other two factors could lead to an overestimation (up to 4-fold) of risk, taken together, they were considered off-setting and not quantitatively factored into the final unit risk value. Using the Mancuso epidemiological data set, US EPA selected the maximum likelihood estimate of the relative risk for the derivation of its unit risk value.

In its analysis of the Mancuso data (1975) for the Air Resources Board (ARB), CDHS (1985) accounted for the hexavalent chromium content, but recommended that possible underestimation of exposure and possible differential smoking patterns not be incorporated into the final unit risk value. Also, CDHS recommended that the 95% upper bound on the "best" estimate of risk be used for the derivation of its unit risk value, which was also accepted by ARB's Scientific Review Panel. These two factors, quantitatively adjusting for the hexavalent chromium content of the total chrome exposure and use of a 95% upper bound value, as compared to a maximum likelihood estimate, may account for most of the differences in unit risk values used by Cal/EPA and US EPA.

Of interest, a 1988 re-evaluation of the CDHS (1985) analysis resulted in selecting the same unit risk value. Both US EPA and Cal/EPA apply their unit risk factors to the hexavalent chromium fraction of an environmental sample. While this

results in over a twelve-fold difference in risk calculations, there is considerable uncertainty in both unit risk values. Fortunately, a new study is currently underway between Johns Hopkins University and the US EPA that is evaluating a much larger worker population with better exposure data. The results of this study may help to resolve some of the differences and uncertainties in the unit risk values.

1,2-Dibromoethane (Ethylene Dibromide)

The US EPA oral estimate is greater, by a factor of 24, than the Cal/EPA estimate. Derivation of the oral cancer potency for this compound is difficult because of the variable bioassay exposure and abbreviated study length, as well as substantial early mortality and high tumor yields observed in the available oral bioassays on the compound. The differences between Cal/EPA and US EPA reflect different approaches for addressing this problem as well as concerns over overestimation that result from applying these approaches.

The US EPA estimate was entered on IRIS in 1987. EPA used a model of Thorslund (1982) which is similar to the Weibull-in-time multistage-in-dose approach. The potency selected (85 $[mg/kg\text{-}day]^{-1}$) was derived from the dose-response data for squamous cell carcinomas of the forestomach from the NCI gavage bioassay on the male Osborne Mendel rat.

The Cal/EPA estimate was reported by CDHS in two documents in 1988. The Weibull-in-time multistage-in-dose model was fitted to tumor dose-response data from gavage bioassays conducted by the NCI on B6C3F1 mice and Osborne Mendel rats of both sexes. A quantitative analysis indicated that the largest potency values estimated may be inconsistent with data from a human occupational study. In part due to concern over possible overestimation, potency was taken as the geometric mean of potencies derived from data for squamous cell tumors in each of the species/sex bioassays of the NCI. The potencies selected for averaging were based on analyses that assumed that the tumors were rapidly lethal.

Epichlorohydrin

The oral cancer potency value of US EPA was last reviewed in 1986. It is a factor of 8 lower than that of Cal/EPA, which was derived by CDHS in 1988. The estimates for both agencies are derived from the dose-response data - forestomach tumors observed in a 81-week drinking water study of male Wistar rats (Konishi et al., 1980). The discrepancy is due to the differences in 1) adjustment made to account for the half life of epichlorohydrin in water in the Konishi et al. experiment (US EPA did not adjust; accounts for a factor of 1.6 difference); and 2) the dose adjustment to account for interspecies differences (The US EPA adjustments appear erroneous and resulted in no correction for interpecies differences, whereas CDHS used surface area scaling; accounts for a factor of 5-6 difference).

Inhalation unit risk factors of US EPA (last reviewed in 1986) and Cal/EPA (derived by CDHS in 1988) also differ significantly for epichlorohydrin. The US EPA estimate is based on the low dose tumor dose-response data in the inhalation study of Laskin et al. who treated Sprague Dawley rats and observed a relatively high incidence of rare nasal tumors in high dose animals. The data on which US EPA based its potency determination are as follows: control group - 0/150 (0 animals with tumor of 150 treated); 10 ppm in air - 0/100; 30 ppm in air - 1/100. US EPA noted that the historical incidence in this case was 0/1920.

CDHS did not find the Laskin et al. study reliable because survival of treated animals was so poor, with 82% of the animals in the 30 ppm group and 74% of the animals in the 10 ppm group dying by the mean time to tumor observed in the high dose group. CDHS noted that since thirty 6-hour exposures to 100 ppm produced roughly 10 times the incidence as lifetime exposure to 30 ppm, the dose-rate response relationship appears to be highly non-linear. However, since data on individual animals was unavailable and the survival in the study was so poor, the study was seen as unreliable for cancer potency estimation. CDHS noted that the value derived from the oral study is consistent with an upper-bound estimate derived from human epidemiological data, and thus decided to adopt the oral value for both inhalation and oral routes until such time as an inhalation study more suitable for potency derivation becomes available.

Pentachlorophenol

The US EPA oral cancer potency is derived from tests of two different preparations of pentachlorophenol. Results for female mice with hemangiosarcomas at any site, or benign or malignant pheochromocytomas or liver tumors were used in the analysis. US EPA employed surface area scaling in extrapolating from the animal studies to humans. The data sets selected for analysis were, for tests of two different preparations of pentachlorophenol, results for female mice with hemangiosarcomas at any site, or benign or malignant pheochromocytomas or liver tumors.

The value provided in Attachment B-4 for Cal/EPA was derived by the Department of Toxic Substances Control (DTSC) for use at hazardous waste sites and differs from US EPA primarily because it assumes doses are equivalent across species on an amount per body weight, rather than amount per surface area basis. The Cal/EPA OEHHA drinking water program recently reevaluated the cancer potency analysis for pentachlorophenol and proposed a value of 0.158 $[mg/kg\text{-}day]^{-1}$ in its March 1994 draft *Recommended Public Health Level for Pentachlorophenol in Drinking Water*. The value recommended is based on the NTP (1989) results for male mice with liver adenoma or carcinoma fed Dowicide EC-7, and accounts for species differences by surface area scaling. This value, which is nearly the same as the US EPA estimate, will be considered for use agency-wide when finalized.

2,4,6-Trichlorophenol

The US EPA cancer potency value (0.011 [mg/kg-day]$^{-1}$) is about a factor of 7 lower than the Cal/EPA estimate (0.07 [mg/kg-day]$^{-1}$) derived in 1988 by CDHS. US EPA applied the linearized multistage procedure to leukemia data in male rats from the 1979 NCI dietary study. Cal/EPA derived potency estimates from the available bioassay data, and noted that the more sensitive study appeared to be that in mice by Innes et al. (1978). The lower 95% confidence bound on cancer potency derived from the Innes et al. data in female mice for hepatomas exceeded the upper confidence bound derived from the NCI dietary study for liver tumors in female mice. Because neither the NCI nor the Innes et al. study appeared to be more suitable for potency estimation, CDHS selected the geometric mean of potencies estimated from 4 data sets - the most sensitive tumor sites for male and female mice in the Innes et al. and NCI studies.

IV. Identification of Chemicals that Have a Substantial Impact on Site-Specific Risk Assessment Results

The top 10 "risk drivers" in Cal/EPA site-specific risk assessments in order of importance are listed in the table below, and the basis for the US EPA and Cal/EPA cancer potency estimates for these compounds is described in the subsequent text.

Hazardous Waste Program	**Air Toxics "Hot Spots" Program**
1. Trichloroethylene (TCE)	1. Chromium VI
2. Perchloroethylene (PCE)	2. Perchloroethylene (PCE)
3. Chlorinated dioxins and dibenzofurans	3. Benzene
4. Lead	4. PAHs
5. Chromium VI	5. Methylene chloride
6. Benzene	6. Arsenic
7. Carcinogenic PAHs	7. Formaldehyde
8. Cadmium	8. Cadmium
9. Nickel	9. Nickel
10. Pentachlorophenol	10. Chlorinated dioxins and dibenzofurans

Arsenic (inorganic)

The primary concern driving the assessments is cancer risk from inhalation exposure. The US EPA and Cal/EPA inhalation unit risk values differ by a small amount; US EPA's estimate is slightly higher, by a factor of 1.3. Both are based on epidemiological studies of lung cancer in smelter workers.

The US EPA estimate was published in 1984 and last verified by the agency workgroup for inclusion on IRIS in February 1994. The unit risk adopted (4.3×10^{-3}

[$\mu g/m^3]^{-1}$) is a geometric mean of 2 risk estimates derived for 2 different smelters. The estimate at one smelter is the geometric mean of 3 values (2 different analysis of one epidemiological data set (Lee-Feldstein, 1983), and one analysis of a different data set (Walsh et al. 1982)); the value for the second smelter is a geometric mean of two analyses of the same study population (Enterline and Marsh, 1982) corresponding to two different assumptions regarding latency period. Because linear models were found to fit better than quadratic models and absolute models fit better than relative risk forms, the individual unit risk estimates were derived using a linear absolute risk model. The measure of exposure used in the analysis was cumulative exposure.

The Cal/EPA value ($3.3x10^{-3}$ [$\mu g/m^3]^{-1}$) was derived by CDHS (1990) who considered the available epidemiological data, including studies evaluated by US EPA and available updated versions. CDHS found the updated version of one study (the Enterline et al., 1987 update of Enterline and Marsh, 1982) most suitable for the derivation of the unit risk, as it was the best one available in terms of ascertainment of exposure, size of study population and person years of follow-up. In its analysis, CDHS accounted for smoking-arsenic interaction and derived separate unit risks for four categories of smoking, and used the California age-specific all-cause and lung cancer mortality rates for 1982 to construct lifetables (US EPA used US 1976 rates).

Benzene

Inhalation or oral risk estimates for benzene can drive the risk estimates at hazardous waste facilities. The US EPA cancer potency of 0.029 $(mg/kg\text{-}day)^{-1}$; or $8.3x10^{-6}$ $(\mu g/m^3)^{-1}$, is the geometric mean of 4 maximum likelihood estimates corresponding to 4 different analyses of pooled human leukemia incidence data from 2 occupational studies (Ott et al., 1978; Rinsky et al., 1981). An adjustment pooled data set was made to account for a similar study by Wong *et al.* (1983): "The results of the Wong *et al.* (1983) study were incorporated by assuming that the ratio of the Rinsky-Ott-Wong studies to the Rinsky-Ott studies for the relative risk cumulative dose model was the same as for other model-exposure category combinations and multiplying this ratio by the Rinsky-Ott geometric mean. [US EPA IRIS, 1987]." Equal weight was given to cumulative dose and weighted cumulative dose exposure categories as well as to relative and absolute risk model forms. In discussing potency selection, the US EPA (1985) noted that the most credible was that derived from the Rinsky et al. data set under the "weighted cumulative dose relative risk model."

The Cal/EPA estimate (0.1 $[mg/kg\text{-}day]^{-1}$; $2.9x10^{-5}$ [$\mu g/m^3]^{-1}$) corresponds to the upper 95% confidence bound derived by US EPA for their "most credible" analysis. It was adopted by CDHS in 1991 and is used to estimate risks for both oral and inhalation exposures. It falls within the range of estimates identified by CDHS (1984) in their evaluation of the available animal bioassay and epidemiological data (0.03 to 0.2 $[mg/kg\text{-}day]^{-1}$).

Cadmium

Significant cancer risks from exposure to cadmium via inhalation can be estimated at facilities that release cadmium into the air and from hazardous waste facilities. The Cal/EPA and US EPA inhalation unit risks for cadmium differ by a factor of 2.3. Both the US EPA and Cal/EPA based their estimates on updates of a NIOSH occupational mortality study of workers at a cadmium production plant in Globe Colorado, reported in 1985 and 1986 by Thun et al. The US EPA applied a linear additive risk model to the data set and selected the maximum likelihood estimate. CDHS (1990) fit a relative risk model to the 1986 update, corrected for the healthy worker effect and selected the upper 95% confidence value on the slope parameter. The primary reason for the difference between the CDHS and US EPA values was parameter selection (i.e., the use of the maximum likelihood versus the upper confidence 95% bound on the slope parameter).

Chlorinated dioxins and dibenzofurans

Food chain exposures to chlorinated dioxins and dibenzofurans drives the cancer risk assessment at facilities that release these chemicals into the air and from hazardous waste sites. US EPA has removed inhalation and oral unit risk values from IRIS, while the agency's dioxin assessment undergoes review and further development. The Cal/EPA values for 2,3,7,8- tetrachlorodibenzo-p-dioxin and 1,2,3,6,7,8- and 1,2,3,7,8,9-hexachlorodibenzo-p-dioxin (HCDD) were derived by CDHS in 1986. The TCDD value was derived by applying the linearized multistage procedure to NTP dose-response data for liver tumor in male mice administered TCDD orally. The estimate for the HCDDs was based on liver tumors observed in female rats receiving the HCDDs by gavage in a second NTP study. Potency estimates for several other chlorinated dioxins and dibenzofurans are derived by applying the International Toxicity Equivalency Factors to the CDHS TCDD and HCDD estimates (which are quite similar to the US EPA estimates removed from IRIS).

Chloroform

The inhalation unit risk values derived by Cal/EPA and US EPA differ by a factor of 4.3 and estimates of cancer potencies for oral exposure by these two agencies differ by a factor of 5.1. Differences between the Cal/EPA and US EPA values are primarily due to the selection of bioassay data sets on which to base the potency estimates.

The US EPA oral cancer potency (0.0061 $[\text{mg/kg-day}]^{-1}$) was derived by applying the linearized multistage procedure to the kidney-tumor data from the drinking water study in male Osborne Mendel rats reported by Jorgensen et al. (1985). The US EPA inhalation unit risk was derived from dose-response data for liver carcinoma in the gavage study in female mice reported by NCI (1976). The latest US EPA review of the inhalation and oral values on US EPA IRIS was conducted in 1987.

The Cal/EPA oral value (0.031 [mg/kg-day]$^{-1}$) was derived in 1990. Cancer potency estimates were derived from several oral studies and included consideration of dose-dependent pharmacokinetics through a PBPK ("physiologically-based phamacokinetic") model. The best estimate is a weighted average of 13 cancer potency estimates corresponding to 13 different oral experiments in mice and rats. The results for the liver tumors in mice observed in the NCI corn oil gavage study were excluded due to the possibility that the production of the tumors was vehicle dependent. Potencies derived from the male rat kidney tumors reported by Jorgensen et al. and by the NCI were weighted most heavily because these were judged to be the more reliable results for potency estimation. The Cal/EPA inhalation value (0.019 [mg/kg-day]$^{-1}$, or 5.3×10^{-6} [μg/m3] $^{-1}$) was derived in the same fashion after taking into account differences in pharmacokinetics between the oral and inhalation route.

Chromium (hexavalent)

The primary concern in site-specific risk assessments is cancer from inhalation exposure to hexavalent chromium. The US EPA and Cal/EPA inhalation unit risks differ by a factor of 12.5. The CDHS (1985) value and US EPA (1984) value were both based on the dose response for lung cancer in chromate production workers, as reported by Mancuso (1975).

In deriving the unit risk value, US EPA (1984) took into consideration that one-seventh (14%) of the total chrome was hexavalent chromium, that 1949 industrial hygiene data may have underestimated exposures, and that chromate workers were likely to have had a higher smoking rate than white males in the general population. Because the first factor could lead to an underestimation (approximately 7-fold) of risk and the other two factors could lead to an overestimation (up to 4-fold) of risk, taken together, they were considered off-setting and not quantitatively factored into the final unit risk value. Using the Mancuso epidemiological data set, US EPA selected the maximum likelihood estimate of the relative risk for the derivation of its unit risk value.

In its analysis of the Mancuso data (1975) for the ARB, CDHS (1985) accounted for the hexavalent chromium content, but recommended that possible underestimation of exposure and possible differential smoking patterns not be incorporated into the final unit risk value. Also, CDHS recommended that the 95% upper bound on the "best" estimate of risk be used for the derivation of its unit risk value, which was also adopted by ARB's Scientific Review Panel. These two factors, quantitatively adjusting for the hexavalent chromium content of the total chrome exposure and use of a 95% upper bound value, as compared to a maximum likelihood estimate, may account for most of the differences in unit risk values used by Cal/EPA and US EPA.

Of interest, a 1988 re-evaluation of the CDHS (1985) analysis resulted in selecting the same unit risk value. Both US EPA and Cal/EPA apply their unit risk factors to the hexavalent chromium fraction of an environmental sample. While this results in over a twelve-fold difference in risk calculations, there is considerable uncertainty in both unit risk values. Fortunately, a new study is currently underway

between Johns Hopkins University and the US EPA that is evaluating a much larger worker population with better exposure data. The results of this study may help to resolve some of the differences and uncertainties in the unit risk values.

Formaldehyde

Cancer risks from the inhalation of formaldehyde drive some of the Air Toxics risk assessments. Cal/EPA and US EPA values differ by a factor of approximately 2. US EPA (1987) developed an inhalation unit risk for formaldehyde from a rat and mouse inhalation bioassays performed for the Chemical Industry Institute of Toxicology (CIIT) (Kerns *et al*., 1983). A linear multistage model was fit to incidence data for squamous cell carcinoma of the nasal cavity in the male rat. A risk of 1.3×10^{-5} $(\mu g/m^3)^{-1}$ was derived. The Cal/EPA estimate was recently derived by OEHHA (1992) who used the CIIT rat bioassay data to calculate a unit risk of 6.0×10^{-6} $(\mu g/m^3)^{-1}$. The reasons for the difference between the Cal/EPA and US EPA values are as follows:

(1) Cal/EPA used the rate of binding of formaldehyde to DNA in the nasal lining of the rat, to characterize the dose rate, whereas US EPA used administered dose.

(2) Cal/EPA used intake rate per body surface area for scaling across species, whereas US EPA assumed that exposure of different species to the same concentration in air would lead to the same cancer lifetime cancer incidence (accounts for a factor of 1.2 difference between the two estimates).

(3) Cal/EPA explicitly accounted for the potential effect of formaldehyde-induced cell proliferation on cancer in deriving a range of risk estimates. Cell proliferation models could increase the estimate of unit risk by 30 to 50 fold, or decrease it by 5.3-fold.

Lead

The primary concern for Cal/EPA site-specific assessments has been non-cancer impacts of lead. Both DTSC of Cal/EPA and US EPA use a lead model to estimate the health hazards associated to exposure to lead in the environment. The model takes into account the concentration of lead in the surrounding media (food, air, soil, and water) of the human receptor. It then calculates the level of lead in blood using the current knowledge on human exposure, absorption , distribution, and excretion of lead by the body. For children exposed to lead, both Cal/EPA and US EPA uses 10 ng of lead per dl of whole blood as the level of concern.

Methylene chloride

Inhaled methylene chloride contributes significantly to risk estimates calculated in some risk assessments performed under the Air Toxics “Hot Spots” program. The Cal/EPA value for inhalation risk (1.0×10^{-6} $[\mu g/m^3]^{-1}$) is approximately twice the US EPA value (4.7×10^{-7} $[\mu g/m^3]^{-1}$). Both US EPA and Cal/EPA OEHHA accounted for dose dependent differences in pharmacokinetics (using a “physiologically based

pharmacokinetic" (PBPK) model) in their derivation of inhalation unit risk values. The US EPA based their estimate on the dose-response data set for combined incidence of liver and lung tumors in an inhalation study in female mice (NTP, 1986). The Cal/EPA value is based on female lung tumor data from the same study. The difference between the Cal/EPA and US EPA estimates is due primarily to differences in application and assumptions regarding pharmacokinetics.

Nickel

Risks from inhaled nickel are a primary concern in some Cal/EPA site-specific risk analyses. US EPA and Cal/EPA have adopted nearly identical values, and based their estimates on human occupational studies of nickel refineries. In 1987, US EPA published their estimate which is based on a range of values derived by fitting dose-response functions to data sets from 4 different refineries (Huntington, WV (Enterline and Marsh, 1982), Copper Cliff, Ontario (Chovil *et al*., 1981), Clydach, Wales (Peto *et al*., 1984), and Kristians and, Norway (Magnus *et al*., 1982)). Both the additive and multiplicative excess risk models were fitted whenever possible, and two types of relative risk models were used. The unit risk estimates ranged from 1.1×10^{-5} to 4.6×10^{-4} $(\mu g/m^3)^{-1}$. As the best estimate, the midpoint of the range, 2.4×10^{-4} $(\mu g/m^3)^{-1}$, was taken as the incremental unit risk due to a lifetime exposure to nickel refinery dust.

The Cal/EPA estimate is based on a CDHS (1990) analysis. CDHS used an updated version of the Ontario cohort study (ICNCM, 1990) since it had the best exposure data. A relative risk model was applied and a unit risk of 2.6×10^{-4} $(\mu g/m^3)^{-1}$ was estimated for nickel. This unit risk is applied to estimate inhalation risk for both soluble and insoluble nickel compounds.

Pentachlorophenol

The US EPA oral cancer potency is derived from tests of two different preparations of pentachlorophenol. Results for female mice with hemangiosarcomas at any site, or benign or malignant pheochromocytomas or liver tumors were used in the analysis. US EPA employed surface area scaling in extrapolating from the animal studies to humans.

The value provided in Attachment B-4 for Cal/EPA was derived by the DTSC for use at hazardous waste sites and differs from US EPA primarily because it assumes doses are equivalent across species on an amount per body weight, rather than amount per surface area basis. The Cal/EPA OEHHA drinking water program has recently reevaluated the cancer potency analysis for pentachlorophenol and has proposed a value of 0.158 $(mg/kg\text{-}day)^{-1}$ in its March 1994 draft *Recommended Public Health Level for Pentachlorophenol in Drinking Water*. The value recommended is based on the NTP (1989) results for male mice with liver adenoma or carcinoma fed Dowicide EC-7, and accounts for species differences by surface area scaling. This value, which is nearly the same as the US EPA estimate, will be considered for agency-wide use when finalized.

Perchloroethylene

Significant risk estimates can be derived for inhalation exposure to perchloroethylene at facilities that release the chemical into the air and oral and inhalation exposures from hazardous waste sites. US EPA has removed its unit risk estimates from the IRIS data base. The Cal/EPA estimate was derived in 1992 and utilizes a PBPK model to account for dose, route and species dependent differences in pharmacokinetics.

Trichloroethylene

Significant risk estimates can be derived for inhalation exposure to trichloroethylene at facilities that release the chemical into the air and oral and inhalation exposures from hazardous waste sites. US EPA has removed its unit risk estimates from the IRIS data base. The Cal/EPA estimate was derived by CDHS in 1990 and utilizes a PBPK model to account for dose, route and species dependent differences in pharmacokinetics.

V. Adjustment/Uncertainty Factors Used in the Development of Health-Based Drinking Water Guidance Levels

Adjustment and uncertainty factors are used to compensate for limitations or deficiencies in the toxicity data available and to adjust for extrapolating health effects observed under one set of conditions to another. The magnitude of these factors and the way they are used in deriving noncancer toxicity values are similar in Cal/EPA and US EPA. For example, a factor of 10 is often used to extrapolate from a Lowest-Observed-Adverse-Effect Level (LOAEL) to No-Observed-Adverse-Effect Level (NOAEL), 10 to account for interspecies difference and an additional 10 for sensitive individuals. Attachment B-5 describes the NOAEL or LOAEL that was used as the basis in deriving de minimis levels for contaminants in drinking water. The attachment also lists the adjustment and uncertainty factors used in each derivation.

Attachment B-1

Tabulated Chronic Oral Toxicity Values Used by Cal/EPA and US EPA for Their Drinking Water Programs (Including Group C Carcinogens)

Chemical	Oral RfD (mg/kg-day)		Ratio of Cal/EPA value to US EPA value
	Cal/EPA	US EPA	
Metals and Inorganic Compounds			
Aluminum	1.8E-01	NA	NA
Antimony	4.3E-04	4.3E-04	1.00
Barium	2.1E-02	7.0E-02	0.30
Beryllium	5.4E-04	5.4E-04	1.00
Cadmium	5.0E-04	5.0E-04	1.00
Chlorate	3.0E-02#	NA	NA
Chlorine Dioxide	3.0E-04#	NA	NA
Chlorite	3.0E-04#	NA	NA
Copper	1.9E-02	3.8E-02 **	0.50
Cyanide	2.1E-02	2.1E-02	1.00
Mercury	3.0E-04	NA	NA
Nickel	2.0E-02	2.0E-02	1.00
Nitrate	1.6E+00	1.6E+00	1.00
Nitrite	1.0E-01	1.0E-01	1.00
Selenium	2.7E-03	2.7E-03	1.00
Silver	5.0E-03#	5.0E-03	1.00
Thallium	8.0E-05	8.0E-05	1.00
Uranium	2.0E-03	3.0E-03	0.67
Organic Compounds			
Chloromethane (Methyl chloride)	1.6E-02#	NA	NA
Chloropicrin	3.7E-03#	NA	NA
1,2-Dichlorobenzene (o-DCB)	9.0E-02	9.0E-02	1.00
1,4-Dichlorobenzene (p-DCB)	1.1E-01***	1.1E-01	1.00
1,1-Dichloroethane (1,1-DCA)	2.7E-03	NA	NA
1,1-Dichloroethylene (1,1-DCE, VDC)	9.0E-04	9.0E-04	1.00
cis-1,2-Dichloroethylene (cis-1,2-DCE)	8.5E-04	1.0E-02 **	0.09
trans-1,2-Dichloroethylene (trans-1,2-DCE)	1.7E-03	1.7E-02	0.10
Dichlorodifluoromethane (Freon 12)	1.5E-01	NA	NA
Ethylbenzene	1.0E-01	1.0E-01	1.00
Methyl-tert-butyl ether (MTBE)	5.0E-03	NA	NA
Monochlorobenzene (Chlorobenzene)	2.0E-02	2.0E-02	1.00
Styrene	2.0E-01	2.0E-01	1.00

Chemical	Oral RfD (mg/kg-day)		Ratio of Cal/EPA value to US EPA value
	Cal/EPA	US EPA	
1,1,2,2-Tetrachloroethane (1,1,2,2-TCA)	1.4E-04	NA ***	NA
Toluene	1.1E-01	2.2E-01	0.50
1,2,4-Trichlorobenzene	1.5E-02	1.5E-02	1.00
1,1,1-Trichloroethane (1,1,1-TCA)	3.0E-02	3.0E-02	1.00
1,1,2-Trichloroethane (1,1,2-TCA)	3.9E-04	3.9E-04	1.00
Trichlorofluoromethane (Freon 11)	1.9E-01	3.5E-01 *	0.54
1,1,2-Trichloro-1,2,2-Trifluoroethane (Freon 113)	2.6E+00	2.7E+01 *	0.10
Xylenes (o, m, p)	2.5E-01	2.0E+00	0.13
Pesticides			
Aldicarb	1.0E-03#	1.0E-03	1.00
Aldicarb Sulfone	1.0E-03#	1.0E-03	1.00
Aldicarb Sulfoxide	1.0E-03#	1.0E-03	1.00
Atrazine	3.5E-04	3.5E-04	1.00
Bentazon	2.5E-03	2.5E-03 *	1.00
Carbofuran	2.6E-03	5.0E-03	0.52
Dalapon	5.0E-02	5.0E-02	1.00
2,4-Dichlorophenoxy acetic acid (2,4-D)	1.0E-02	1.0E-02	1.00
Di(2-ethylhexyl)adipate (DEHA)	5.7E-02	5.7E-02	1.00
Dinoseb	1.0E-03	1.0E-03	1.00
Diquat	2.2E-03	2.2E-03	1.00
Endothall	2.0E-02	2.0E-02	1.00
Endrin	2.5E-04	2.5E-04	1.00
Glyphosate	1.0E-01	1.0E-01	1.00
Hexachlorocyclopentadiene (HEX)	1.0E-02	1.0E-02	1.00
Methoxychlor	5.0E-03	5.0E-03	1.00
Molinate (Ordam)	2.0E-03	2.0E-03 *	1.00
Oxamyl (Vydate)	2.5E-02	2.5E-02	1.00
Picloram	7.0E-02	7.0E-02	1.00
Simazine	5.0E-04	5.0E-04	1.00
Thiobencarb (Bolero)	1.0E-02	1.0E-02 *	1.00
2,4,5-TP (Silvex)	7.5E-03	7.5E-03	1.00

NA = Not Available
# Currently under review, a new value may be developed.
* MCLG has not been established but RfD is available in the current IRIS.
** MCLG has been established but RfD is under review in the current IRIS.
*** Group C carcinogen, standard has been established based on carcinogenicity.

Attachment B-2

Tabulated Chronic Inhalation Toxicity Values Used by Cal/EPA for the Air Toxics "Hot Spots" Program and by US EPA

Chemical	Chronic Inhalation Toxicity Value ($\mu g/m^3$) (1)		Ratio of Cal/EPA value to US EPA value
	Cal/EPA, REL	US EPA, RfC	
Acetaldehyde	9.0E+00	9.0E+00	1.00
Acrolein	2.0E-02	2.0E-02	1.00
Acrylamide	7.0E-01 (a)	NA	NA
Acrylonitrile	2.0E+00	2.0E+00	1.00
Ammonia	1.0E+02	1.0E+02	1.00
Arsenic	5.0E-01	NA	NA
Benzene	7.1E+01	NA	NA
Benzidine (and its salts)	1.0E+01 (a)	NA	NA
Benzyl chloride	1.2E+01	NA	NA
Beryllium	4.8E-03	NA	NA
Bromine	1.7E+00	NA	NA
Bromine compounds			
Hydrogen bromide	2.4E+01	NA	NA
Bromine pentafluoride	1.7E+00	NA	NA
Cadmium	3.5E+00 (a)	NA	NA
Carbon tetrachloride	2.4E+00 (a)	NA	NA
Chlorinated dibenzo-p-dioxins (as 2,3,7,8-equivalents)	3.5E-06 (a)	NA	NA
Chlorinated dibenzofurans (as 2,3,7,8-equivalents)	3.5E-06 (a)	NA	NA
Chlorine	7.1E+00	NA	NA
Chlorobenzene (monochlorobenzene)	7.0E+01 (a)	NA	NA
Chlorofluorocarbons	7.0E+02 (a)	NA	NA
Chloroform	3.5E+01 (a)	NA	NA
Chlorophenols			
2-Chlorophenol	1.8E+01	NA	NA
Pentachlorophenol	2.0E-01	NA	NA
Tetrachlorophenols	8.8E+01	NA	NA
Chloropicrin	1.7E+00	NA	NA
Chloroprene	1.0E+00	NA	NA
Chromium (hexavalent)	2.0E-03	NA	NA
Copper	2.4E+00	NA	NA
Cresols (o, m, p)	1.8E+02	NA	NA
1,2-Dibromo-3-chloropropane (DBCP)	2.0E-01	2.0E-01	1.00
p-Dichlorobenzene (1,4-Dichlorobenzene)	7.0E+02	8.0E+02	0.88
1,4-Dioxane	4.0E+02	NA	NA
Di(2-ethylhexyl)phthalate	7.0E+01 (a)	NA	NA

Chemical	Chronic Inhalation Toxicity Value (μg/m^3) (1)		Ratio of Cal/EPA value to US EPA value
	Cal/EPA, REL	US EPA, RfC	
Dimethylamine	2.0E+00	NA	NA
Epichlorohydrin	3.0E-01	1.0E+00	0.30
Ethyl acrylate	4.8E+01	NA	NA
Ethyl chloride	1.0E+04	1.0E+04	1.00
Ethylene dibromide (1,2-Dibromoethane)	4.6E+00	NA	NA
Ethylene dichloride (1,2-Dichloroethane)	9.5E+01	NA	NA
Ethylene glycol butyl ether	2.0E+01	NA	NA
Ethylene glycol monoethyl ether	2.0E+02	2.0E+02	1.00
Ethylene glycol ethyl ether acetate	6.4E+01	NA	NA
Ethylene glycol methyl ether	2.0E+01	2.0E+01	1.00
Ethylene glycol methyl ether acetate	5.7E+01	NA	NA
Ethylene oxide	6.0E+02	NA	NA
Formaldehyde	3.6E+00	NA	NA
gamma-Hexachlorocyclohexane	1.0E+00 (a)	NA	NA
Gasoline vapors	2.1E+03	NA	NA
Glutaraldehyde	1.7E+00	NA	NA
Hexachlorobenzene	2.8E+00 (a)	NA	NA
Hexachlorocyclopentadiene	2.4E-01	NA	NA
Hydrazine	2.4E-01	NA	NA
Hydrochloric acid	7.0E+00	2.0E+01	0.35
Hydrogen cyanide	7.0E+01 (a)	3.0E+00	23.33
Hydrogen fluoride	5.9E+00	NA	NA
Hydrogen sulfide	4.2E+01	1.0E+00	42.00
Isocyanates			
2,4-/2,6-Toluene diisocyanate mixture	9.5E-02	7.0E-02	1.36
Methyl isocyanate	3.6E-01	NA	NA
Lead and compounds	1.5E+00	NA	NA
Maleic anhydride	2.4E+00	NA	NA
Manganese and compounds	4.0E-01	5.0E-02	8.00
Mercury and compounds (inorganic)	3.0E-01	3.0E-01	1.00
Methanol	6.2E+02	NA	NA
Methyl bromide (Bromomethane)	6.0E+00	5.0E+00	1.20
Methyl chloroform (1,1,1-TCA)	3.2E+02 (a)	NA	NA
Methylene chloride	3.0E+03	NA	NA
4,4'-Methylene dianiline (and its dichloride)	1.9E+00	NA	NA
Methyl mercury	1.0E+00 (a)	NA	NA
Methyl methacrylate	9.8E+02	NA	NA
Mineral fibers (< 1% free silica)	2.4E+01	NA	NA
Naphthalene	1.4E+01 (a)	NA	NA
Nickel and nickel compounds	2.4E-01	NA	NA
Nitrobenzene	1.7E+00 (a)	NA	NA
Nitrogen dioxide	4.7E+02	1.0E+02 (b)	4.70

Chemical	Chronic Inhalation Toxicity Value (μg/m^3) (1)		Ratio of Cal/EPA value to US EPA value
	Cal/EPA, REL	US EPA, RfC	
2-Nitropropane	2.0E+01	2.0E+01	1.00
Ozone	1.8E+02	NA	NA
Perchloroethylene (Tetrachloroethylene)	3.5E+01 (a)	NA	NA
Phenol	4.5E+01	NA	NA
Phosphine	1.0E+01 (a)	3.0E-01	33.33
Phosphorous (white)	7.0E-02 (a)	NA	NA
Phthalic anhydride	7.0E+03 (a)	NA	NA
PCBs (Polychlorinated biphenyls)	1.2E+00	NA	NA
Propylene oxide	3.0E+01	3.0E+01	1.00
Selenium compounds	5.0E-01	NA	NA
Sodium hydroxide	4.8E+00	NA	NA
Styrene	7.0E+02 (a)	1.0E+03	0.70
Sulfates	2.5E+01	NA	NA
Sulfur dioxide	1.3E+02 (c)	8.0E+01 (b)	1.63
Toluene	2.0E+02	4.0E+02	0.50
Trichloroethylene	6.4E+02	NA	NA
Vinyl chloride	2.6E+01 (a)	NA	NA
Vinylidene chloride	3.2E+01	NA	NA
Xylenes	3.0E+02	NA	NA
Zinc compounds	3.5E+01	NA	NA

(1) Cal/EPA Reference Exposure Levels (RELs) reported in CAPCOA (1993) and US EPA Reference Concentrations (RfCs) reported in IRIS (1995).

(a) Values derived from oral acceptable exposure levels (mg/kg-day) by assuming a 70 kg person breathes 20 cubic meters of air per day and equal absorption occurs by the inhalation and oral route.

(b) NAAQS = National Ambient Air Quality Standards would be used by US EPA in place of a chronic RfC.

(c) The chronic value of 660 μg/m^3 listed in the CAPCOA (1993) is the acute CAPCOA REL and is a typographical error. The actual value should have been 130 μg/m^3. This value was adopted from the 24-hour California Ambient Air Qualtiy Standard for sulfur dioxide.

NA = Not Available

Attachment B-3

Tabulated Toxicity Values Used by Cal/EPA and US EPA for their Pesticide Programs

[The information presented below addresses numerical differences between chronic and/or acute NOELs established by DPR, Cal/EPA and US EPA]

Comparison of Acute No-Observed-Effect Levels (NOELs) Developed by Department of Pesticide Regulation and US EPA

Pesticide	DPR NOEL[a] (mg/kg-day)	US EPA NOEL[b] (mg/kg-day)		Comments
		Dietary (1 day)	Occupational (1-7 days)	
Alachlor	N.A.[c]		400	DPR acute exposure not assessed
Amitraz	0.125[d]	0.125	0.125	Same study, same NOEL
Amitrole	4.0		4.0	No food use
Avermectin B1	0.05	0.06	0.05	
Azinphos-methyl	1.0	1.0	0.14	
Benomyl	(11.4)[e]	10	30	
Bensulfuron methyl	35			
Bifenthrin	1.0		1.0	
Chlorpyrifos	0.5			
Clofentezine	1000			
Cyanazine	1.0			
Cycloate	20			
Cyhexatin	0.5			
Cyromazine	5.0		30	
DEF	25.4			
1,3-Dichloropropene	54.8			
Dichlorvos	0.5	0.5		

a These values represent the current status and could be revised with the consideration of additional data.
b These values were provided by US EPA (OPP) (10/31/95).
c N.A. = Not available
d Human study
e NOEL values in parentheses were estimated from LOEL values using an uncertainty factor of 10.

Comparison of Acute No-Observed-Effect Levels (NOELs) Developed by Department of Pesticide Regulation and US EPA for Selected Pesticides (continued)

Pesticide	DPR NOEL[a] (mg/kg-day)	US EPA NOEL[b] (mg/kg-day)		Comments
		Dietary (1 day)	Occupational (1-7 days)	
Diflubenzuron	N.A. [c]	10,000	40	DPR acute exposure not assessed
Diquat	(0.3)		20 (dermal) 19.9 (inhalation)	
EPTC	20			
Ethoprop	2.0			
Ethyl parathion	0.1			
Fenamiphos	0.23	0.5		
Fenoxaprop-ethyl	10	10 [f]		
Fenpropathrin	6.0		4.0	
Flutolanil	N.A.	40	40	DPR acute exposure not assessed
Folpet	(15.0)			
Fosetyl Al	1,000		125	
Hydrogen cyanamide	5.0		6.0	
Imidacloprid	10	24		
Malathion	(0.34)[d]			
Metalaxyl	50			
Methyl bromide	5.0		14.5	
Methyl parathion	0.31[d]	0.31[d, g]		

a These values represent the current status and could be revised with the consideration of additional data.
b These values were provided by US EPA (OPP) (10/31/95).
c N.A. = Not available
d Human study
e NOEL values in parentheses were estimated from LOEL values using an uncertainty factor of 10.
f NOEL from US EPA Drinking Water Health Advisory.
g US EPA Drinking Water Health Advisory, uncertainty factor=10.

Comparison of Acute No-Observed-Effect Levels (NOELs) Developed by Department of Pesticide Regulation and US EPA for Selected Pesticides (continued)

Pesticide	DPR NOEL[a] (mg/kg-day)	US EPA NOEL[b] (mg/kg-day)		Comments
		Dietary (1 day)	Occupational (1-7 days)	
Mevinphos	0.025[d]	0.025		
Molinate	11.5			
Monocrotophos	(1.7)			
Myclobutanil	31		>100	
Paclobutrazol	10			
Permethrin	50			
Phosmet	10	1.1	1.1	
Propaconazole	30		30	
Tralomethrin	(0.01)[f]		8	
Triadimefon	20		20	

a These values represent the current status and could be revised with the consideration of additional data.
b These values were provided by US EPA (OPP) (10/31/95).
c N.A. = Not available
d Human study
e NOEL values in parentheses were estimated from LOEL values using an uncertainty factor of 10.
f Subsequent to the development of this information, additional data were submitted which resulted in a revision of the acute NOEL for tralomethrin from 0.01 mg/kg to 1.0 mg/kg (1996).

Comparison of Chronic No Observed Effect Levels (NOELs) and Reference Doses (RfDs) Developed by Department of Pesticide Regulation and US EPA for Selected Pesticides

Pesticide	DPR NOEL[a] (mg/kg-day)	DPR RfD[b] (mg/kg-day)	US EPA NOEL[c] (mg/kg-day)	US EPA RfD[c] (mg/kg-day)	Comments[d]
Alachlor	3	0.03	1	0.01	SS, DN
Amitraz	(0.23)[e]	0.0023	0.25	0.0025	DS, DN
Amitrole	0.244[f]	0.0244	N.A.[g]	N.A.	No US EPA RfD No Food Use
Avermectin B1	0.12	0.0012	0.12	0.0004	SS, SN
Azinphos-methyl	0.28	0.0028	0.15	0.0015	DS, DN
Benomyl	3.5[h] 5.5[i]	0.035 0.055	5	0.05	DS, DN
Bensulfuron methyl	19.9	0.2	19.9	0.2	SS, SN
Bifenthrin	N.A.	N.A.	1.5	0.015	No DPR Chronic NOEL, Just Oncogenicity
Captafol	2.9	0.029	(0.2)	0.002	DS, DN
Chlorpyrifos	1.0	0.01	0.03	0.003	DS, DN
Clofentezine	0.43	0.0043	1.25	0.013	DS, DN
Cyanazine	0.2	0.002	0.2	0.002	SS, SN
Cycloate	0.5	0.005	0.5	0.005	SS, SN
Cyhexatin	(0.1)	0.001	(0.075)	0.00075	DS, DN
Cyromazine	1.7	0.017	0.75	0.0075	DS, DN
DEF	0.2	0.002	0.1	0.00003	DS, DN
1,3-dichloro-propene	6.7 (5 ppm)	0.067	---------- (5 ppm)	---------- 0.02 mg/m^3 (RfC)	SS, SN DPR and US EPA have same oncogenicity Q_1

a These values represent the current status and could be revised with the consideration of additional data.
b DPR does not generally calculate an RfD by dividing the NOEL by a prescribed uncertainty factor (UF); however, for comparative purposes, the RfDs in this column were obtained by dividing the DPR NOEL by 100, the conventional UF used by US EPA.
c Obtained from RfD Tracking Report (US EPA, OPP September, 1995).
d SS = same study, DS = different study, SN = same NOEL, DN = different NOEL.
e NOEL values in parentheses were estimated from LOEL values using an UF of 10.
f Human study.
g N.A. = information not available.
h Adjusted NOEL for dermal, inhalation routes.
i NOEL for dietary (oral).

Comparison of Chronic No Observed Effect Levels (NOELs) and Reference Doses (RfDs) Developed by Department of Pesticide Regulation and US EPA for Selected Pesticides (continued)

Pesticide	DPR NOEL[a] (mg/kg-day)	DPR RfD[b] (mg/kg-day)	US EPA NOEL[c] (mg/kg-day)	US EPA RfD[c] (mg/kg-day)	Comments[d]
Dichlorvos	0.05	0.0005	0.05	0.0005	SS, SN
Diflubenzuron	1.3	0.013	2	0.02	DS, DN
Diquat dibromide	0.50	0.005	0.5	0.005	SS, SN
EPTC	0.5	0.005	2.5	0.025	DS, DN
Ethoprop	0.025	0.00025 UF=100	0.015	0.000015 UF=1000	DS, DN
Ethyl parathion	0.4	0.004	(0.001)	0.00033	DS, DN
Fenamiphos	0.5	0.005	0.01	0.0001	DS, DN
Fenoxaprop-ethyl	0.9	0.009	0.25	0.0025	DS, DN
Fenpropathrin	3.0	0.03	2.5	0.025	SS, SN
Folpet	15	0.15	10	0.1	DS, DN
Fosetyl-Al	250	2.5	250	3	SS, SN
Hydrogen cyanamide	0.2	0.002	0.2	0.002	SS, SN
Imidacloprid	5.7	0.057	5.7	0.057	SS, SN
Isofenphos	0.5	0.005	0.05	0.0005	SS, DN
Malathion	0.34[f]	0.0034	0.23	0.02	SS, DN
Metalaxyl	3.4	0.034	7.41	0.074	DS, DN
Methyl parathion	0.02	0.0002	0.025	0.00025	DS, DN
Mevinphos	0.025	0.00025	0.025	0.00025	DS, SN

a These values represent the current status and could be revised with the consideration of additional information.
b DPR does not generally calculate an RfD by dividing the NOEL by a prescribed uncertainty factor (UF); however, for comparative purposes the RfD's in this column were obtained by dividing the DPR NOEL by 100, the conventional UF used by US EPA.
c Obtained from RfD tracking report (US EPA, OPP, September, 1995)
d SS = same study, DS = different study, SN = same NOEL, DN = different NOEL
e NOEL values in parentheses were estimated from LOEL values using an uncertainty factor of 10.
f Human study; uncertainty factor is still 100 because NOEL from subcrhonic study
g N.A. = information not available

Comparison of Chronic No Observed Effect Levels (NOELs) and Reference Doses (RfDs) Developed by Department of Pesticide Regulation and US EPA for Selected Pesticides (continued)

Pesticide	DPR NOEL[a] (mg/kg-day)	DPR RfD[b] (mg/kg-day)	US EPA NOEL[c] (mg/kg-day)	US EPA RfD[c] (mg/kg-day)	Comments[d]
Molinate	1	0.01	0.2	0.002	DS, DN
Monocrotophos	0.05	0.0005	0.0045	0.00005	DS, DN
Myclobutanil	2.5	0.025	2.5	0.025	SS, SN
Paclobutrazol	1.6	0.016	2.5	0.025	DS, DN
Permethrin	3	0.03	5	0.05	DS, DN
Phosmet	2.0	0.02	2.0	0.02	SS, SN
Tralomethrin	(0.075)	0.00075	0.75	0.0075	DS, DN
Triadimefon	2.5	0.025	11.4	0.04	DS, DN

a These values represent the current status and could be revised with the consideration of additional information.
b DPR does not generally calculate an RfD by dividing the NOEL by a prescribed uncertainty factor (UF); however, for comparative purposes the RfD's in this column were obtained by dividing the DPR NOEL by 100, the conventional UF used by US EPA.
c Obtained from RfD tracking report (US EPA, OPP, September, 1995)
d SS = same study, DS = different study, SN = same NOEL, DN = different NOEL
e NOEL values in parentheses were estimated from LOEL values using an uncertainty factor of 10.
f Human study; uncertainty factor is still 100 because NOEL from subcrhonic study
g N.A. = information not available

Comparison and Explanation of NOELs Established by Cal/EPA and US EPA

[The information presented below addresses numerical differences between chronic and/or acute NOELs established by DPR, Cal/EPA and US EPA [a]]

AMITRAZ

Chronic NOEL

US EPA (1993*)
US EPA established a NOEL of 0.25 mg/kg-day on the basis of increased blood glucose and slight hypothermia after dosing (LOEL was 1 mg/kg-day), in a two-year feeding study with dogs.

DPR (1995++)
In the same two-year dog study, DPR noted that all treated dogs exhibited central nervous system (CNS) effects within 3 hours after dosing. No other treatment-related effects were noted. Since the effects were considered acute, the chronic NOEL for this study was set at 1 mg/kg-day (highest dose tested).
In a chronic feeding study with mice, DPR noted an increase in liver hyperplastic nodules and forestomach hyperkeratosis. The LOEL was 2.3 mg/kg-day. DPR estimated a NOEL of 0.23 mg/kg-day by using a default procedure of dividing the LOEL by an uncertainty factor of 10.

Conclusion: DPR used 0.23 mg/kg-day as the NOEL to assess chronic exposure.

Acute NOEL

US EPA
On the basis of the CNS effects reported in humans at 0.25 mg/kg, the NOEL was determined by US EPA to be 0.125 mg/kg-day.
Note: The acute NOEL of 0.25 mg/kg-day initially listed in the comparison table was incorrect. The current value used by US EPA in their Reregistration Eligibility Document (RED) is 0.125 mg/kg-day.

DPR
DPR used the same human study as US EPA and also established the critical acute NOEL at 0.125 mg/kg-day, based on CNS effects.

Conclusion: As a result of the current harmonization project, both US EPA and DPR have established the critical acute NOEL at 0.125 mg/kg-day.

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a These values represent the current status and could be revised with the consideration of additional data

* Date of latest US EPA review
** Date of latest entry in IRIS
\+ Date of completed DPR risk assessment
++ Date of draft DPR risk assessment

AZINPHOSMETHYL

Chronic NOEL

US EPA (1986*)
US EPA established a critical chronic NOEL of 0.15 mg/kg-day based on diarrhea (cholinergic sign) and erythrocyte cholinesterase inhibition in a one-year dog feeding study. DPR considered the effect of diarrhea at the next higher dose of 0.7 mg/kg-day equivocal and identified 0.7 mg/kg-day as the NOEL for this study based on significant brain cholinesterase inhibition and diarrhea at 4.1 mg/kg-day.

DPR (1995++)
DPR established a critical chronic NOEL of 0.28 mg/kg-day based on reduced body weight and brain cholinesterase inhibition in a two-year rat feeding study.

Conclusion: DPR used 0.28 mg/kg-day as the NOEL to assess chronic dietary and occupational exposures.

BENOMYL

Chronic NOEL

US EPA (1986*)
US EPA established the critical chronic NOEL at 5 mg/kg-day based on decreased body weight in rat pups in a three-generation reproduction study.

DPR (1995++)
DPR established the critical chronic NOEL at 5.5 mg/kg-day based on hepatotoxicity in a one-year dog feeding study.

Conclusion: DPR used 5.5 mg/kg-day as the NOEL to assess chronic dietary and an adjusted NOEL of 3.5 mg/kg-day (based on 64% oral absorption[b]) to assess chronic exposure from dermal or inhalation routes for occupational exposures.

Acute NOEL

US EPA (1995*)
US EPA established a critical acute NOEL at 30 mg/kg-day for occupational exposure (1-7 days) based on fetal microphthalmia in a rat developmental toxicity study. US EPA also established a one-day dietary NOEL of 10 mg/kg-day based on an increase in fetal developmental variations in a rat developmental toxicity study. Both studies where submitted to US EPA by the registrant for benomyl.

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b When oral absorption data are submitted or can be calculated from pharmacokinetic data, DPR will generally adjust an oral NOEL when the gastrointestinal absorption is less than 100% and when the oral exposure is used as a surrogate to estimate the systemic dosage from other potential routes (e.g. dermal, inhalation) of exposure. It is generally assumed that gastrointestinal absorption is equivalent across species, including humans; therefore, an oral NOEL from an animal study is not adjusted in assessing potential human dietary exposure.

DPR (1995++)
DPR established a preliminary critical acute NOEL at 11.4 mg/kg-day (estimated) based on the sloughing of germinal epithelium after a single oral dose of 114 mg/kg-day in a rat reproduction study which was published in the open literature.

Conclusion: DPR used 11.4 mg/kg-day to assess acute dietary and occupational exposures.

CHLORPYRIFOS

Chronic NOEL

US EPA (1995*)
US EPA established a critical chronic NOEL at 0.03 mg/kg-day based on the inhibition of plasma cholinesterase in a 20 day human study. DPR does not consider the endpoint (plasma cholinesterase inhibition) a toxicologically significant effect[c], and 20 days is not generally sufficient to constitute chronic exposure. Therefore, DPR did not use this study to establish a critical chronic NOEL.

DPR (1992+)
DPR established the critical chronic NOEL at 1 mg/kg-day based on the inhibition of brain cholinesterase at one year in dog and rat feeding studies.

Conclusion: DPR used 1 mg/kg-day as the NOEL to assess chronic dietary, residential and occupational exposures.

CLOFENTEZINE

Chronic NOEL

US EPA (1986*,1993**)
US EPA established the critical chronic NOEL of 1.25 mg/kg-day (50 ppm) based on liver biochemistry, liver histopathology and increased organ weight in a one-year dog feeding study. DPR also selected 50 ppm as the NOEL for this study.

DPR (1991+)
DPR established the critical chronic NOEL at 0.43 mg/kg-day (10 ppm) based on thyroid hyperplasia/neoplasia in a rat feeding study. US EPA selected the next higher dose, 40 ppm, as the NOEL for this study based on the thyroid and liver effects.

Conclusion: DPR used 0.43 mg/kg-day as the critical NOEL for assessing chronic exposure.

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c *In the absence of cholinergic signs and/or brain cholinesterase inhibition, DPR does not consider plasma or erythrocyte cholinesterase inhibition per se as a toxicologically significant effect on which to established a critical NOEL for risk assessment.*

CYROMAZINE

Chronic NOEL

US EPA (1986*,1991**)
The RfD was set at 0.0075 mg/kg-day based on a NOEL of 0.75 mg/kg-day (30 ppm) in a 6-month dog feeding study. The endpoints were decreased hematocrit and hemoglobin.
(Note: In establishing the NOEL at 0.75 mg/kg-day, EPA used a default assumption that food consumption was 2.5% of body weight (i.e. 1 ppm=0.025 mg/kg-day). The NOEL based on actual food consumption data presented in the study was 0.9 mg/kg-day for males and females.)

DPR concluded that the NOEL in the dog study was at the next higher dose (300 ppm) (i.e., 9.27 mg/kg-day/males; 8.85 mg/kg-day/females) based on statistically significant decreases in hematocrit and hemoglobin, as well as bilateral degeneration of the seminiferous tubules and decreased spermatogenesis at 3000 ppm.

DPR (1993*)
DPR established the critical chronic NOEL at 1.7 mg/kg-day (30 ppm) based on a significant decrease in mean body weight gain in a rat reproduction study. In addition, a NOEL was established at 1.8 mg/kg-day for decreased body weight gain in a two-year rat feeding study.
US EPA also set the NOEL at 1.7 mg/kg-day in the rat reproduction study.

Conclusion: DPR used 1.7 mg/kg-day as the critical NOEL for assessing chronic exposure.

Acute NOEL

US EPA (1995*,1991**)
The current critical acute NOEL is 30 mg/kg-day based on developmental toxicity in a rabbit teratology study. US EPA initially (1985) established a NOEL for developmental toxicity at 5 mg/kg-day based on malformations (cyclopia and diaphragmatic hernia) at 10 mg/kg-day. The NOEL for maternal toxicity was 10 mg/kg-day. In 1989 US EPA changed the NOEL for developmental toxicity based on a reexamination of the original data and various issues (e.g. historical control) surrounding the incidence of cyclopia. US EPA has subsequently raised the NOEL to 30 mg/kg-day.

DPR (1993+)
DPR has maintained that the maternal NOEL in the rabbit study was 10 mg/kg-day, and the NOEL for developmental toxicity was at the low dose of 5 mg/kg-day, based primarily on cyclopia. DPR reviewed the information and arguments presented by US EPA to support changing the NOEL from 5 to 10 mg/kg-day and did not concur with their interpretation or conclusions.

Conclusion: A NOEL of 5 mg/kg-day was used by DPR to assess acute dietary, residential and occupational exposures.

DEF

Chronic NOEL

US EPA (1987*)

US EPA calculated the RfD of 0.00003 mg/kg-day based on an oral NOEL of 0.1 mg/kg-day from a 90-day neurotoxicity study in hens in which ataxia, delayed neuropathy and weight loss were seen. An uncertainty factor of 3,000 was used, but the rationale for this factor was not available. A 1,000-fold uncertainty factor may have been used to extrapolate from a subchronic exposure to chronic exposure. The additional uncertainty factor of 3 may have been applied because of either species used or the severity of the endpoint.

DPR (1995++)

DPR had concerns with both the acceptability of the subchronic oral hen study and the difference between the NOEL of this study and other subchronic neurotoxicity studies which had NOELs at least 10-fold higher. Because of these concerns and the presence of acceptable chronic studies in three species, the chronic NOEL of 0.2 mg/kg-day was selected based on hyperplasia and vacuolar degeneration in the small intestine and hematological changes observed in rats exposed to DEF in the diet for two years.

1,3-DICHLOROPROPENE

Chronic NOEL

US EPA (1987*)

US EPA calculated the RfC of 0.02 mg/m^3 based on an inhalation NOEL of 5 ppm (6 hr/day, 5 days/week) established in a two-year mice study. The effects observed in female mice at the LOEL of 20 ppm were: respiratory epithelium hyperplasia and hypertrophy, and hyperplasia of urinary bladder mucosa. The NOEL of 3 mg/kg-day that appeared in the previous version was established in a 90-day feeding study in rats based on increased relative kidney weight. It was used for the calculation of the RfD.

DPR (1994+)

DPR also established the chronic inhalation NOEL at 5 ppm. The dose of 6.7 mg/kg-day was calculated based on the purity of 92.1% and default breathing rate of 1.8 m^3/kg-day for mice without the adjustment of inhalation absorption.

Conclusion: Both DPR and US EPA assessed the chronic/lifetime exposures based on oncogenic effects.

DIFLUBENZURON

Chronic NOEL

US EPA (1986*,1992**)

US EPA established the critical chronic NOEL of 2 mg/kg-day based on methemoglobinemia in a one-year dog feeding study. DPR also established the NOEL in this study at 2 mg/kg-day.

DPR (1987+)

Note: The chronic NOEL of 5.6 mg/kg-day initially listed in the comparison table was incorrect. The value should be 1.3 mg/kg-day based on methemoglobinemia in a chronic mouse feeding study.

Conclusion: DPR used a NOEL of 1.3 mg/kg-day to assess chronic exposures.

DIQUAT

Chronic NOEL

US EPA (1994*)
US EPA established the critical chronic NOEL at 0.5 mg/kg-day based on cataracts in a one-year dog feeding study.

DPR (1993**)
Note: The chronic NOEL of 0.66 mg/kg-day initially listed in the comparison table was incorrect. The value should be 0.5 mg/kg-day based on the same endpoint (cataracts) and study (dog) used by US EPA.

Conclusion: DPR used 0.5 mg/kg-day as the NOEL to assess chronic oral exposures. Since there is pharmacokinetic data indicating that the gastrointestinal absorption of diquat in the rat is approximately 10%, an adjusted chronic NOEL of 0.05 mg/kg-day would be used to assess other potential routes of exposure.

Acute NOEL

US EPA (1995*)
Note: The acute value of 40 mg/kg-day initially presented in the comparison table was the LOEL and not the NOEL. US EPA established an acute dermal NOEL of 20 mg/kg-day based on weakness, unsteadiness and weight loss in a rabbit 21 day exposure study. US EPA also established an acute inhalation NOEL of 19.9 mg/kg-day (0.1 g/L) based on lung lesions in rats after 21 days of exposure. US EPA did not established an acute oral NOEL.

DPR (1993++)
Note: The acute NOEL of 0.1 mg/kg-day initially listed in the comparison table was incorrect. The value should be 0.3 mg/kg-day (estimated) based on developmental abnormalities in a rat developmental toxicity study.

Conclusion: DPR used 0.3 mg/kg-day as the NOEL to assess acute oral exposures. Since there is pharmacokinetic data indicating that the gastrointestinal absorption of diquat in the rat is approximately 10%, an adjusted acute NOEL of 0.03 mg/kg-day would be used to assess other potential routes of exposure.

EPTC

Chronic NOEL

US EPA (1987*)

US EPA established a critical chronic NOEL of 2.5 mg/kg-day based on degenerative cardiomyopathy in a rat reproduction study.

DPR (1993++)
DPR established a critical chronic NOEL (estimated) of 0.5 mg/kg-day based on neuromuscular degeneration in a two-year rat feeding study. This effect was present at all doses including the lowest dose of 5 mg/kg-day; therefore, DPR, using a default procedure of dividing the LOEL by 10, calculated an estimated NOEL of 0.5 mg/kg-day.

Conclusion: DPR used 0.5 mg/kg-day as the NOEL to assess chronic exposures.

ETHOPROP

Chronic NOEL

US EPA (1986*)
US EPA established a critical chronic NOEL at 0.015 mg/kg-day based on decreased adrenal gland weight and erythrocyte and brain cholinesterase inhibition in a 90 day rat feeding study[d].

DPR (1995++)
DPR established a critical chronic NOEL at 0.025 mg/kg-day based on centrolobular vacuolation, focal necrosis, periportal fibrosis and/or biliary proliferation in a one-year dog oral study.

Conclusion: DPR used 0.025 mg/kg-day as the NOEL to assess chronic exposure.

FENAMIPHOS

Chronic NOEL

US EPA (1993*)
US EPA established a critical chronic NOEL of 0.01 mg/kg-day (0.5 ppm) based on the inhibition of plasma cholinesterase activity in a one year dog feeding study. DPR established NOELs of 0.03 mg/kg-day and 0.09 mg/kg-day for the inhibition of plasma and brain cholinesterase, respectively, in the same dog study.

DPR (1992+)
DPR established a critical chronic NOEL of 0.5 mg/kg-day in a two-year rat feeding study based on systemic toxicity (inflammatory lesions of the nasal, laryngeal and lung tissues) and brain cholinesterase inhibition.

Conclusion: DPR used 0.5 mg/kg-day as the NOEL to assess chronic dietary exposures.

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d DPR considers a 90 day toxicity study as a subchronic study and does not generally use a subchronic study to establish a critical chronic NOEL when an acceptable chronic study is available

Acute NOEL

US EPA (1995*)
US EPA, using a developmental toxicity study, established a NOEL of 0.5 mg/kg-day (nominal concentration) based on cholinergic signs in maternal rabbits.

DPR (1992+)
Fenamiphos has a tendency to degrade in aqueous media; therefore, the NOEL established by DPR for cholinergic signs in the same rabbit developmental toxicity study was based on measured concentrations of the dosing solutions and not on the nominal concentrations.
The acute NOEL established by DPR was 0.23 mg/kg-day.

Conclusion: DPR used 0.23 mg/kg-day as the NOEL to assess acute exposures.

FENOXAPROP-ETHYL

Chronic NOEL

US EPA
US EPA established a critical chronic NOEL of 0.25 mg/kg-day based on reduced blood lipids in parents and reduced body weight in pups in a rat reproduction study. DPR set the NOEL for the rat reproduction study at 1.7 mg/kg-day based on reduced pup weight (statistically significant only at next higher dose), increased relative liver and kidney weights and decreased absolute thymus weight in the parents.

DPR
DPR established the critical chronic NOEL at 0.9 mg/kg-day based reduced absolute body weight, reduced body weight gain and increased relative liver weight in a two-year dog study.

Conclusion: DPR used 0.9 mg/kg-day as the NOEL to assess chronic exposures.

Acute NOEL

US EPA
US EPA established the critical acute NOEL at 10 mg/kg-day based on abortions, fetal anomalies and growth retardation observed at 50 mg/kg-day in a rabbit developmental toxicity study. DPR, on the other hand, using a combination of two developmental studies by the same investigators, selected 50 mg/kg-day as the NOEL for developmental toxicity observed at 200 mg/kg-day in one of the rabbit studies.

DPR
DPR established the same value, 10 mg/kg-day, as the critical acute NOEL; however, the endpoints were increased fetal anomalies in a rat reproduction study and an increased incidence of mortality in pregnant Cynomolgus monkeys at 50 mg/kg-day.

Conclusion: DPR used 10 mg/kg-day as the NOEL to assess acute exposures.

FENPROPATHRIN

Chronic NOEL

US EPA (1993*)
US EPA established the chronic NOEL at 100 ppm (2.5 mg/kg-day) on the basis of tremors reported in a one-year feeding study with dogs.

DPR (1994+)
In the same dog feeding study, DPR determined that the chronic NOEL was also 100 ppm based on tremors; however, the calculated dosage used by DPR was 3 mg/kg-day. This minor difference in dosage from US EPA is probably the result of default assumptions used for food consumption.
Note: The chronic NOEL of 3.1 mg/kg-day initially listed in the comparison table was incorrect. The value should be 3.0 mg/kg-day based on tremors in the dog study.

Conclusion: DPR used 3.0 mg/kg-day as the NOEL to assess chronic dietary and occupational exposures.

Acute NOEL

US EPA
US EPA established an acute oral NOEL of 4 mg/kg-day based on maternal toxicity in a rabbit developmental toxicity study.

DPR
Two NOELs were established by DPR for estimating margins of safety for acute exposure to fenpropathrin. A NOEL of 32 mg/kg-day, based on ataxia, tremors, and hypersensitivity reported in acute dermal LD_{50} studies conducted in rats and mice was established for dermal exposure, primarily under occupational settings. Additionally, a NOEL of 6 mg/kg-day, based on death, convulsions, ataxia, and tremors, reported in a rat developmental study was used to assess oral or inhalation exposures.

Conclusion: DPR used 32 mg/kg-day as the NOEL to assess acute dermal exposures and 6 mg/kg-day as the NOEL to assess acute oral or inhalation exposures.

IMIDACLOPRID

Acute NOEL

US EPA (1995*)
US EPA established a one day acute dietary NOEL of 24 mg/kg-day based on maternal toxicity (increased mortality, abortions, resorptions; decreased body weight) and developmental toxicity (increased skeletal abnormalities) at 72 mg/kg-day.

DPR (1993+)
DPR established the critical acute NOEL at 10 mg/kg-day based on hypoactivity, labored breathing, tremors and apathy in mice given a single oral dose.

Conclusion: DPR used 10 mg/kg-day as the NOEL to assess acute exposures.

ISOFENPHOS

Chronic NOEL

US EPA (1994*)
US EPA established the critical chronic NOEL at 0.05 mg/kg-day (1 ppm) based on erythrocyte cholinesterase inhibition in a two-year rat feeding study.

DPR (1991+)

In the review of the same rat feeding study, DPR concurred with US EPA in establishing the NOEL for erythrocyte cholinesterase inhibition at 1 ppm. However, in the absence of cholinergic signs or symptoms at 0.5 mg/kg-day, the critical NOEL was established at 0.5 mg/kg-day (10 ppm) based on cholinergic signs at the next higher dose of 5 mg/kg-day.

Conclusion: DPR used 0.5 mg/kg-day as the critical NOEL to assess chronic exposures.

MALATHION

Chronic NOEL

US EPA (1987*)
US EPA established the critical chronic NOEL at 0.23 mg/kg-day in a 32-56 day study in humans based on the inhibition of plasma and erythrocyte cholinesterase.

DPR (1993+)
DPR established the chronic NOEL of 0.34 mg/kg-day, the highest dose tested, from the same human study based on the lack of clinical signs of toxicity.

Conclusion: DPR used 0.34 mg/kg-day as the NOEL to assess chronic exposures.

METALAXYL

Chronic NOEL

US EPA (1994*, 1994**)
US EPA established the critical chronic NOEL at 250 ppm based on increased serum alkaline phosphatase levels and increased liver to brain weight ratios in a 6 month dog feeding study. The corresponding dosage for 250 ppm is listed in the current RfD Tracking Report (9/95) as 7.41 mg/kg-day; however, the current entry in IRIS has this dosage as 6.25 mg/kg-day with a corresponding RfD of 0.06 mg/kg-day.

DPR (1991+)
DPR established the critical chronic NOEL at 3.4 mg/kg-day (50 ppm) based on liver cell hypertrophy in a 3-month rat feeding study.

Conclusion: DPR used 3.4 mg/kg-day as the NOEL to assess chronic exposures.

Acute NOEL

DPR (1991+)
Note: The DPR acute NOEL of 1.0 mg/kg-day initially listed in the comparison table was incorrect. The value should be 50 mg/kg-day based on maternal toxicity (convulsions, death, decreased body weight gain) in a rat developmental toxicity study.

METHYL BROMIDE

Acute NOEL

The apparent difference in the acute NOELs listed for DPR and US EPA is because the NOELs were established for different routes of exposure.

US EPA (1995*)
The NOEL of 14.5 mg/kg-day (40 ppm) based on developmental toxicity (gall bladder agenesis, fused sternebrae, decreased fetal body weight) was from a rabbit inhalation study to assess occupational exposure.

DPR (1995++)
DPR is currently using the same rabbit inhalation study, the same endpoints and the same NOEL of 40 ppm to evaluate acute inhalation exposure. However, DPR calculated a dosage of 21 mg/kg-day based on a rabbit respiration rate of 0.54 m^3/kg-d, and US EPA used a respiration rate of 0.37 m^3/kg-d to arrive at their dosage of 14.5 mg/kg-day.
DPR also established a NOEL of 5 mg/kg-day based on clinical signs (hypoactivity, hypothermia, loss of pain reflex) in a dog oral study to assess potential dietary exposures.

Conclusion: DPR used 5 mg/kg-day as the NOEL to assess acute oral exposure and 21 mg/kg-day (40 ppm) as the NOEL to assess acute inhalation exposure.

METHYL PARATHION

Chronic NOEL

US EPA (1986*)
US EPA established the critical chronic NOEL of 0.025 mg/kg-day in a two-year feeding study in rats based on the inhibition of erythrocyte cholinesterase.

DPR (1993++)
DPR established the critical chronic NOEL of 0.02 mg/kg-day in a one-year study in rats based on proximal sciatic and tibial/peroneal nerve myelin degeneration observed at the LOEL of 0.1 mg/kg-day.

Conclusion: DPR used 0.02 mg/kg-day as the NOEL to assess chronic ambient air exposures.

MOLINATE

Chronic NOEL

US EPA (1988*)
US EPA established a critical chronic NOEL of 0.2 mg/kg-day based on sperm abnormalities in a 30-day rat study conducted in 1981. Since the use of molinate as a rice herbicide is truly seasonal, DPR established a seasonal NOEL of 0.48 mg/kg-day based on sperm abnormalities in a subchronic rat study submitted to DPR in 1993.

DPR (1995++)

DPR established a critical chronic NOEL at 1 mg/kg-day based on neurotoxicity in a one-year dog feeding study.

Conclusion: DPR used 1 mg/kg-day as the NOEL to assess chronic exposure and 0.48mg/kg-day as the NOEL to assess seasonal exposure.

MONOCROTOPHOS

Chronic NOEL

US EPA (1986*)
US EPA established a critical chronic NOEL of 0.0045 based on decreased plasma, erythrocyte and brain cholinesterase activities in a two-year rat feeding study.
Note: US EPA canceled the federal registration of monocrotophos.

DPR (1989+)
DPR established a critical chronic NOEL of 0.05 mg/kg-day based increased pre-weaning loss and poor mammary gland development in a rat reproduction study.

Conclusion: DPR used 0.05 mg/kg-day as the NOEL to assess chronic occupational exposures.

PARATHION, ETHYL

Chronic NOEL

US EPA (1986*)
US EPA established the LOEL of 0.01 mg/kg-day in a one-year feeding study in dogs based on the inhibition of plasma and erythrocyte cholinesterase. Using a default UF of 10, the estimated NOEL was 0.001 mg/kg-day.

DPR (1992+)
DPR established the chronic NOEL of 0.4 mg/kg-day in a two-year feeding study in rats based on ocular effects, tremors, and body weight reduction observed at 1.6 mg/kg-day.

Conclusion: DPR used 0.4 mg/kg-day as the NOEL to assess chronic ambient air exposures.

PERMETHRIN

Chronic NOEL

US EPA(1986*)
US EPA established the critical chronic NOEL at 5 mg/kg-day based on increased liver weight in a two-year rat feeding study. In the absence of any histological changes and lack of statistical differences from controls, DPR did not consider this effect as "adverse" and identified the NOEL at 25 mg/kg-day, the highest dose.

DPR (1994+)

DPR established the critical chronic NOEL at 3 mg/kg-day based on alveolar cell proliferation and liver hypertrophy in a two-year mouse feeding study.

Conclusion: DPR used 3 mg/kg-day as the NOEL to assess chronic exposures.

PHOSMET

Chronic NOEL
US EPA (1994*,1992**)
US EPA established a critical chronic NOEL at 20 ppm (~1 mg/kg-day) based on decreased plasma cholinesterase activity in a two-year rat feeding study.

DPR (1988+)
DPR was in agreement with US EPA that the NOEL for plasma cholinesterase inhibition was 20 ppm in the two-year rat feeding study. However, in this study DPR established the critical NOEL at 40 ppm (2 mg/kg-day) based on the inhibition of brain cholinesterase and liver cell vacuolation.

Conclusion: DPR used 2 mg/kg-day as the critical NOEL to assess chronic dietary and occupational exposures.

Acute NOEL

US EPA (1995*)
US EPA established a NOEL of 1.1 mg/kg-day based on erythrocyte/serum cholinesterase inhibition, which occurred at early sampling points, in a two-year rat feeding study for chronic toxicity and oncogenicity.

DPR (1988+)
DPR established the critical acute NOEL at 10 mg/kg-day based on a statistically significant decrease in brain cholinesterase at 4 hours in a rat gavage study.

Conclusion: DPR used 10 mg/kg-day as the NOEL to assess acute exposures.

TRALOMETHRIN

Chronic NOEL

US EPA (1989*)
US EPA established the critical chronic NOEL of 0.75 mg/kg-day in a two-year rat feeding study based on decreased body weight in males, increased food and water consumption in males and females at 3 mg/kg-day.

DPR (1995+)
In the two-year rat feeding study, DPR considered the NOEL to be 3 mg/kg-day based on excessive salivation, uncoordinated movements, and an inability to support weight on limbs at 12 mg/kg-day. In a

two-year feeding study with mice, DPR established a LOEL at 0.75 mg/kg-day, the lowest dose tested, based on chronic dermatitis. DPR calculated an estimated NOEL of 0.075 mg/kg-day by using the default procedure of dividing the LOEL by an uncertainty factor of 10.

Conclusion: DPR used an estimated NOEL of 0.075 mg/kg-day to assess chronic dietary and occupational exposures.

Acute NOEL

US EPA (1995*)
US EPA established an acute NOEL of 8 mg/kg-day to assess occupational exposures. The basis for this NOEL is not currently available from US EPA.

DPR (1995+)
DPR established a LOEL of 0.1 mg/kg-day in a 13 week oral dog study. The basis for the LOEL was autonomic nervous system dysfunction (diarrhea/liquid feces) during the first week of the study. DPR calculated an estimated NOEL of 0.01 mg/kg-day by using the default procedure of dividing the LOEL by an uncertainty factor of 10.

Conclusion: DPR used an estimated NOEL of 0.01 mg/kg-day to assess acute dietary, residential and occupational exposures.[e]

TRIADIMEFON

Chronic NOEL

US EPA (1995*, 1992**)
US EPA initially (1986) established a critical chronic NOEL of 2.5 mg/kg-day (50 ppm) based on decreased body weight, decreased hematological parameters in a two-year rat feeding study. In 1995, US EPA changed the critical chronic NOEL and subsequent RfD to 11.4 mg/kg-day (330 ppm) and 0.04 mg/kg-day, respectively. The NOEL was based on decreased food intake, decreased weight gain and changes in various clinical chemistry parameters in a two-year dog feeding study. An uncertainty factor of 300 was used in establishing the RfD.

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[e] Subsequent to the development of this information, additional data were submitted which resulted in a revision of the acute NOEL for tralomethrin from 0.01 mg/kg to 1.0 mg/kg (1996).

DPR (1992+)
DPR has reviewed (1885, 1992) the two-year dog study and agrees with US EPA that the NOEL for this study is 330 ppm; however, DPR decided to use the NOEL of 2.5 mg/kg-day from the two-year rat study to assess chronic exposure, primarily because the endpoints in the dog study are not considered as more "adverse" than the endpoints in the rat study and the NOEL for the rat study is lower than the NOEL in the dog study.

Conclusion: DPR used 2.5 mg/kg-day as the NOEL to assess chronic exposures.

Comparison of Chronic No Observed Effect Levels (NOELs) and Reference Doses (RfDs) Developed by Department of Pesticide Regulation and US EPA for Selected Pesticides [a]

43 chemicals were listed with either DPR or US EPA chronic NOELs and RfDs

DPR and US EPA established comparative NOELs for 41 of the 43 chemicals

DPR established lower NOELs for 11 of the 41 chemicals

US EPA established lower NOELs for 16 of the 41 chemicals

DPR and US EPA selected the same NOEL for 14 of the 41 chemicals

DPR and US EPA selected a NOEL from the same study for 13 of the 41 chemicals

DPR and US EPA selected the same NOEL for 9 of these 13 chemicals

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a Revised from changes made in the chronic NOEL comparison table

Comparison of Acute No Observed Effect Levels (NOELs) Developed by Department of Pesticide Regulation and US EPA for Selected Pesticides

44 chemicals were listed with either DPR or US EPA acute NOELs

DPR and US EPA established comparative NOELs for 23 of the 44 chemicals

DPR established lower NOELs for 9 of the 23 chemicals

US EPA established lower NOELs for 5 of the 23 chemicals

DPR and US EPA selected the same NOEL for 9 of the 23 chemicals

Attachment B-4

Tabulated Cancer Potency Values Used by Cal/EPA and US EPA

Chemical	Inhalation Unit Risk [µg/m^3]$^{-1}$		Ratio of Cal/EPA value to US EPA value	Oral Unit Risk (mg/kg-day)$^{-1}$		Ratio of Cal/EPA value to US EPA value
	Cal/EPA	US EPA [(a)]		Cal/EPA	US EPA [(a)]	
A-alpha-C (2-Amino-9H-pyrido[2,3-b]indole)	1.1 E-04			4.0 E-01		
Acetaldehyde	2.7 E-06	2.2 E-06	1.2 E+00			
Acetamide	2.0 E-05			7.0 E-02		
Acrylamide	1.3 E-03	1.3 E-03	1.0 E+00	4.5 E+00	4.5 E+00	1.0 E+00
2-Acetylaminofluorene	1.3 E-03			3.8 E+00		
Acrylonitrile	2.9 E-04	6.8 E-05	4.3 E+00	1.0 E+00	5.4 E-01	1.9 E+00
Actinomycin D	2.5 E+00			8.7 E+03		
AF-2 ([2-(2-furyl)-3(nitro-2-furyl)]acrylamide)	6.9 E-05			2.4 E-01		
Aldrin	4.9 E-03	4.9 E-03	1.0 E+00	1.7 E+01	1.7 E+01	1.0 E+00
Allyl chloride	6.0 E-06			2.1 E-02		
2-Aminoanthraquinone	9.4 E-06			3.3 E-02		
ortho-Aminoazotoluene	1.1 E-03			3.8 E+00		
4-Aminobiphenyl (4-aminodiphenyl)	6.0 E-03			2.1 E+01		
3-Amino-9-ethylcarbazole hydrochloride	2.2 E-05			7.8 E-02		
1-Amino-2-methyl-anthraquinone	4.3 E-05			1.5 E-01		
2-Amino-5-(5-nitro-2-furyl)-1,3,4-thiadiazole	4.6 E-03			1.6 E+01		
Amitrole	2.7 E-04			9.4 E-01		
Aniline	1.6 E-06			5.7 E-03	5.7 E-03	1.0 E+00
ortho-Anisidine	4.0 E-05			1.4 E-01		
ortho-Anisidine hydrochloride	3.1 E-05			1.1 E-01		
Aramite	8.6 E-06	7.1 E-06	1.2 E+00	3.0 E-02	2.5 E-02	1.2 E+00
Arsenic, inorganic	3.3 E-03	4.3 E-03	7.7 E-01		1.5 E+00	

Chemical	Inhalation Unit Risk [μg/m^3]$^{-1}$		Ratio of Cal/EPA value to US EPA value	Oral Unit Risk (mg/kg-day)$^{-1}$		Ratio of Cal/EPA value to US EPA value
	Cal/EPA	US EPA [(a)]		Cal/EPA	US EPA [(a)]	
Asbestos	0.00019 per 100 pcm (fib/m^3)	2.3E-1 per (fib/ml)				
Auramine	2.5 E-04			8.8 E-01		
Azaserine	3.1 E-03			1.1 E+01		
Azathioprine	5.1 E-04			1.8 E+00		
Azobenzene	3.1 E-05	3.1 E-05	1.0 E+00	1.1 E-01	1.1 E-01	1.0 E+00
Benz(a)anthracene	PEF Approach (b)			PEF Approach (b)		
Benzene	2.9 E-05	8.3 E-06	3.5 E+00	1.0 E-01	2.9 E-02	3.4 E+00
Benzidine	1.4 E-01	6.7 E-02	2.1 E+00	5.0 E+02	2.3 E+02	2.2 E+00
Benzo(b)fluoranthene	PEF Approach (b)			PEF Approach (b)		
Benzo(j)fluoranthene	PEF Approach (b)			PEF Approach (b)		
Benzo(k)fluoranthene	PEF Approach (b)			PEF Approach (b)		
Benzo(a)pyrene (BaP)	1.1 E-03			1.2 E+01	7.3 E+00	1.6 E+00
Benzyl chloride	4.9 E-05			1.7 E-01	1.7 E-01	1.0 E+00
Benzyl violet 4B	5.7 E-06			2.0 E-02		
Beryllium oxide	2.0 E-03	2.4 E-03	8.3 E-01	7.0 E+00	4.3 E+00	1.6 E+00
Beryllium sulfate	0.86 [(c)]			3.0 E+3 [(c)]		
Bis(2-chloroethyl) ether	7.1 E-04	3.3 E-04	2.2 E+00	2.5 E+00	1.1 E+00	2.3 E+00
Bis(chloromethyl) ether	1.3 E-02	6.2 E-02	2.1 E-01	4.6 E+01	2.2 E+02	2.1 E-01
Bromodichloromethane	3.7 E-05			1.3 E-01	6.2 E-02	2.1 E+00
1,3-Butadiene	1.7 E-04	2.8 E-04	6.1 E-01	3.4 E+00		
Butylated hydroxyanisole	5.7 E-08			2.0 E-04		
beta-Butyrolactone	2.9 E-04			1.0 E+00		
Cadmium	4.2 E-03	1.8 E-03	2.3 E+00			

Chemical	**Inhalation Unit Risk [μg/m^3]$^{-1}$**		**Ratio of Cal/EPA value to US EPA value**	**Oral Unit Risk (mg/kg-day)$^{-1}$**		**Ratio of Cal/EPA value to US EPA value**
	Cal/EPA	**US EPA [(a)]**		**Cal/EPA**	**US EPA [(a)]**	
Captafol	4.3 E-05			1.5 E-01	*(8.6 E-03)*	
Captan	6.6 E-07			2.3 E-03	*(3.5 E-03)*	
Carbon tetrachloride	4.2 E-05	1.5 E-05	2.8 E+00	1.5 E-01	1.3 E-01	1.2 E+00
Chlorambucil	1.3 E-01			2.3 E-03		
Chlordane	3.4 E-04	3.7 E-04	9.2 E-01	1.2 E+00	1.3 E+00	9.2 E-01
Chlordecone (Kepone)	4.6 E-03			1.6 E+01		
Chlorendic acid	2.6 E-05			9.1 E-02		
Chlorinated paraffins (Average chain length, C12: approx.60 percent chlorine by weight)	2.5 E-05			8.9 E-02		
Chlorodibromomethane	2.7 E-05			9.4 E-02		
Chloroform	5.3 E-06	2.3 E-05	2.3 E-01	3.1 E-02	6.1 E-03	5.1 E+00
Chloromethyl methyl ether (technical grade)	6.9 E-04			2.4 E+00		
3-Chloro-2-methylpropene	4.0 E-05			1.4 E-01		
4-Chloro-ortho-phenylenediamine	4.6 E-06			1.6 E-02		
Chlorothalonil	8.9 E-07			4.2 E-01	*(1.1 E-02)*	
p-Chloro-o-toluidine	7.7 E-05			2.7 E-01		
Chlorozotocin	6.9 E-02			2.4 E+02		
Chromium, hexavalent	1.5 E-01	1.2 E-02	1.3 E+01	4.2 E-01		
Chrysene	PEF Approach (b)			PEF Approach (b)		
C. I. Basic Red 9 monohydrochloride	7.1 E-05			2.4 E+02		
Cinnamyl anthranilate	1.3 E-06			4.6 E-03		
Coke oven emissions	6.2 E-04	6.2 E-04	1.0 E+00			
para-Cresidine	4.3 E-05			1.5 E-01		
Cupferron	6.3 E-05			2.2 E-01		
Cyclophosphamide (anhydrous)	1.7 E-04			6.1 E-01		

Chemical	Inhalation Unit Risk [μg/m^3]$^{-1}$		Ratio of Cal/EPA value to US EPA value	Oral Unit Risk (mg/kg-day)$^{-1}$		Ratio of Cal/EPA value to US EPA value
	Cal/EPA	US EPA [(a)]		Cal/EPA	US EPA [(a)]	
Cyclophosphamide (hydrated)	1.6 E-04			5.7 E-01		
D & C Red No. 9	1.5 E-06			5.3 E-03		
Dacarbazine	1.4 E-02			4.9 E+01		
Daminozide	5.1 E-06			1.8 E-02		
Dantron (Chrysazin; 1,8-Dihydroxyanthraquinone)	2.2 E-05			7.6 E-02		
DDD	6.9 E-05			2.4 E-01	2.4 E-01	1.0 E+00
DDE	9.7 E-05			3.4 E-01	3.4 E-01	1.0 E+00
DDT	9.7 E-05	9.7 E-05	1.0 E+00	3.4 E-01	3.4 E-01	1.0 E+00
2,4-Diaminoanisole	6.6 E-06			2.3 E-02		
2,4-Diaminoanisole sulfate	3.7 E-06			1.3 E-02		
4,4'-Diaminodiphenyl ether (4,4'-Oxydianiline)	4.0 E-05			1.4 E-01		
2,4-Diaminotoluene	1.1 E-03			4.0 E+00		
Dibenz(a,j)acridine	PEF Approach (b)			PEF Approach (b)		
Dibenz(ah)acridine	PEF Approach (b)			PEF Approach (b)		
Dibenz[a,h]anthracene	1.2 E-03			4.1 E+00		
7H-dibenzo(c,g)carbazole	PEF Approach (b)			PEF Approach (b)		
Dibenzo(a,e)pyrene	PEF Approach (b)			PEF Approach (b)		
Dibenzo(a,h)pyrene	PEF Approach (b)			PEF Approach (b)		
Dibenzo(a,i)pyrene	PEF Approach (b)			PEF Approach (b)		
Dibenzo(a,l)pyrene	PEF Approach (b)			PEF Approach (b)		
1,2-Dibromo-3-chloropropane (DBCP)	2.0 E-03	*(2.3 E-03)*		7.0 E+00	*(1.4 E+00)*	

Chemical	**Inhalation Unit Risk [μg/m^3]$^{-1}$**		**Ratio of Cal/EPA value to US EPA value**	**Oral Unit Risk (mg/kg-day)$^{-1}$**		**Ratio of Cal/EPA value to US EPA value**
	Cal/EPA	**US EPA [(a)]**		**Cal/EPA**	**US EPA [(a)]**	
1,2-Dibromoethane (Ethylene dibromide)	7.1 E-05	2.2 E-04	3.2 E-01	3.6 E+00	8.5 E+01	4.2 E-02
1,4-Dichlorobenzene	1.1 E-05			4.0 E-02	*(2.4 E-02)*	
3,3'-Dichlorobenzidine	3.4 E-04			1.2 E+00	4.5 E-01	2.7 E+00
1,1-Dichloroethane	1.6 E-06			5.7 E-03		
1,2-Dichloroethane (Ethylene dichloride, EDC)	2.2 E-05	2.6 E-05	8.5 E-01	7.0 E-02	9.1 E-02	7.7 E-01
1,2-Dichloropropane	1.8 E-05			6.3 E-02	*(6.8 E-02)*	
1,3-Dichloropropene (Telone)	1.6 E-05			1.8 E-01	*(1.8 E-01)*	
Dichlorvos (DDVP)	8.3 E-05			4.1 E-01	2.9 E-01	1.4 E+00
Dieldrin	4.6 E-03	4.6 E-03	1.0 E+00	1.6 E+01	1.6 E+01	1.0 E+00
Di(2-ethylhexyl) phthalate (DEHP, Bis(2-ehtylhexyl) phthalate)	2.4 E-06			8.4 E-03		
Diethylstilbestrol	1.0 E-01			3.5 E+02	*(4.7 E+03)*	
Diglycidyl resorcinol ether (DGRE)	4.9 E-04			1.7 E+00		
Dihydrosafrole	1.3 E-05			4.4 E-02		
4-Dimethylaminoazo-benzene	1.3 E-03			4.6 E+00		
trans-2[(Dimethylamino)-methylimino]-5-[2-(5-nitro-2-furyl)-vinyl]-1,3,4-oxadiazole	1.3 E-04			4.4 E-01		
7,12-Dimethylbenz(a)-anthracene	7.1 E-02			2.5 E+02		
Dimethylcarbamyl chloride	3.7 E-03			1.3 E+01		
1,2-Dimethylhydrazine	1.6 E-01			5.5 E+02		
Dimethylvinylchloride	1.3 E-05			4.5 E-02		
1,6-Dinitropyrene	PEF Approach (b)			PEF Approach (b)		
1,8-Dinitropyrene	PEF Approach (b)			PEF Approach (b)		
2,4-Dinitrotoluene	8.9 E-05			3.1 E-01		

Chemical	Inhalation Unit Risk [μg/m^3]$^{-1}$		Ratio of Cal/EPA value to US EPA value	Oral Unit Risk (mg/kg-day)$^{-1}$		Ratio of Cal/EPA value to US EPA value
	Cal/EPA	US EPA [(a)]		Cal/EPA	US EPA [(a)]	
1,4-Dioxane	7.7 E-06			2.7 E-02	1.1 E-02	2.5 E+00
Direct Black 38 (technical grade)	2.1 E-03			7.4 E+00	*(8.6 E+00)*	
Direct Blue 6 (technical grade)	2.1 E-03			7.4 E+00	*(8.1 E+00)*	
Direct Brown 95 (technical grade)	1.9 E-03			6.7 E+00	*(9.3 E+00)*	
Disperse Blue 1 (technical grade)	1.3 E-06			4.5 E-03		
Epichlorohydrin	2.3 E-05	1.2 E-06	1.9 E+01	8.0 E-02	9.9 E-03	8.1 E+00
Estradiol 17B	1.1 E-02			3.9 E+01		
Ethyl-4,4'-dichlorobenzilate (Chlorobenzilate)	3.1 E-05			1.1 E-01		
Ethylene oxide	8.8 E-05	*(1.0 E-04)*		3.1 E-01	*(1.0 E+00)*	
Ethyleneimine	1.9 E-02			6.5 E+01		
Ethylene thiourea	1.3 E-05			4.5 E-02	*(1.1 E-01)*	
Formaldehyde	6.0 E-06	1.3 E-05	4.6 E-01			
2-(2-Formylhydrazino)-4-(5-nitro-2-furyl)thiazole	6.6 E-04			2.3 E+00		
Furmecyclox	8.6 E-06			3.0 E-02	3.0 E-02	1.0 E+00
Glu-P-1 (2-Amino-6-methyl-dipyrido[1,2-a:3',2'-d] imidazole)	1.4 E-03			4.8 E+00		
Glu-P-2 (2-Aminodipyrido[1,2-a:3',2'-d]imidazole)	4.0 E-04			1.4 E+00		
Gyromitrin (Acetaldehyde methylformylhydrazone)	2.9 E-03			1.0 E+01		
HC Blue 1	1.5 E-05			5.1 E-02		
Heptachlor	1.6 E-03	1.3 E-03	1.2 E+00	5.7 E+00	4.5 E+00	1.3 E+00
Heptachlor epoxide	3.7 E-03	2.6 E-03	1.4 E+00	1.3 E+01	9.1 E+00	1.4 E+00
Hexachlorobenzene	5.1 E-04	4.6 E-04	1.1 E+00	1.8 E+00	1.6 E+00	1.1 E+00
Hexachlorocyclohexane (technical grade)	1.1 E-03	5.1 E-04	2.2 E+00	4.0 E+00	1.8 E+00	2.2 E+00
Hexachlorocyclohexane, gamma isomer (Lindane)	3.1 E-04			1.1 E+00	*(1.3 E+00)*	
2,3,7,8-Hexachlorodibenzo-p-dioxin (mixture)	9.4 E-01	1.3 E+00	7.2 E-01	3.3 E+03	6.3 E+03	5.2 E-01

Chemical	**Inhalation Unit Risk [μg/m^3]$^{-1}$**		**Ratio of Cal/EPA value to US EPA value**	**Oral Unit Risk (mg/kg-day)$^{-1}$**		**Ratio of Cal/EPA value to US EPA value**
	Cal/EPA	**US EPA [(a)]**		**Cal/EPA**	**US EPA [(a)]**	
Hexachloroethane	1.1 E-05	4.0 E-06	2.8 E+00	3.9 E-02	1.4 E-02	2.8 E+00
Hydrazobenzene (1,2-Diphenylhydrazine)	2.5 E-04			8.7 E-01		
Hydrazine	4.9 E-03	4.9 E-03	1.0 E+00	1.7 E+01		
Hydrazine sulfate	8.6 E-04			3.0 E+00	3.0 E+00	1.0 E+00
Indeno(1,2,3-c,d)pyrene	PEF Approach (b)			PEF Approach (b)		
IQ (2-Amino-3-methyl-imidazo[4,5-f]quinoline)	4.0 E-04			1.4 E+00		
Lasiocarpine	2.2 E-03			7.8 E+00		
Lead acetate	8.0 E-05			2.8 E-01		
Lead subacetate	1.1 E-05			3.8 E-02		
Me-A-alpha-C (2-Amino-3-methyl-9H-pyrido [2,3-b]indole)	3.4 E-04			1.2 E+00		
Melphalan	3.7 E-02			1.3 E+02		
3-Methylcholanthrene	6.3 E-03			2.2 E+01		
5-methylchrysene	PEF Approach (b)			PEF Approach (b)		
4,4'-Methylene bis(2-chloro-aniline)	4.3 E-04	*(3.7 E-05)*		1.5 E+00	*(1.3 E-01)*	
4,4'-Methylene bis(2-methylaniline)	2.6 E-04			9.2 E-01		
4,4'-Methylene bis(N,N'-dimethyl)aniline	1.3 E-05			4.6 E-02	4.6 E-02	1.0 E+00
Methylene chloride	1.0 E-06	4.7 E-07	2.1 E+00	1.4 E-02	7.5 E-03	1.9 E+00
4,4'-Methylenedianiline	4.6 E-04			1.6 E+00		
4,4'-Methylenedianiline dihydrochloride	3.4 E-04			1.2 E+00		
Methyl methanesulfonate	2.8 E-05			9.9 E-02		
2-Methyl-1-nitroanthraquinone (of uncertain purity)	1.2 E-03			4.3 E+00		
N-Methyl-N'-nitro-N-nitrosoguanidine	2.4 E-03			8.3 E+00		
Methylthiouracil	1.1 E-04			4.0 E-01		

Chemical	**Inhalation Unit Risk [μg/m^3]$^{-1}$**		**Ratio of Cal/EPA value to US EPA value**	**Oral Unit Risk (mg/kg-day)$^{-1}$**		**Ratio of Cal/EPA value to US EPA value**
	Cal/EPA	**US EPA [(a)]**		**Cal/EPA**	**US EPA [(a)]**	
Michler's ketone	2.5 E-04			8.6 E-01		
Mirex	5.1 E-03			1.8 E+01		
Mitomycin C	2.3 E+00			8.2 E+03		
Monocrotaline	2.9 E-03			1.0 E+01		
2-Naphthylamine				1.8 E+00		
Nickel and Nickel compounds [(d)]	2.6 E-04	2.4 E-04	1.1 E+00			
Nickel subsulfide	4.9 E-04	4.8 E-04	1.0 E+00	1.7 E+00		
Nitrilotriacetic acid	1.5 E-06			5.3 E-03		
Nitrilotriacetic acid, trisodium salt monohydrate	2.9 E-06			1.0 E-02		
5-Nitroacenaphthene	3.7 E-05			1.3 E-01		
5-Nitro-o-anisidine	1.4 E-05			4.9 E-02		
6-Nitrochrysene	PEF Approach (b)			PEF Approach (b)		
Nitrofen (technical grade)	2.3 E-05			8.2 E-02		
2-Nitrofluorene	PEF Approach (b)			PEF Approach (b)		
Nitrofurazone	3.7 E-04			1.3 E+00	*(1.5 E+00)*	
1-[(5-Nitrofurfurylidene)-amino]-2-imidazolidinone	5.1 E-04			1.8 E+00		
N-[4-(5-Nitro-2-furyl)-2-thiazolyl]-acetamide	4.3 E-04			1.5 E+00		
1-Nitropyrene	PEF Approach (b)			PEF Approach (b)		
4-Nitropyrene	PEF Approach (b)			PEF Approach (b)		
N-Nitrosodi-n-butylamine	3.1 E-03	1.6 E-03	1.9 E+00	1.1 E+01	5.4 E+00	2.0 E+00
N-Nitrosodiethanolamine	8.0 E-04			2.8 E+00	2.8 E+00	1.0 E+00
N-Nitrosodiethylamine	1.0 E-02	4.3 E-02	2.3 E-01	3.6 E+01	1.5 E+02	2.4 E-01

Chemical	Inhalation Unit Risk [μg/m^3]$^{-1}$		Ratio of Cal/EPA value to US EPA value	Oral Unit Risk (mg/kg-day)$^{-1}$		Ratio of Cal/EPA value to US EPA value
	Cal/EPA	US EPA [(a)]		Cal/EPA	US EPA [(a)]	
N-Nitrosodimethylamine	4.6 E-03	1.4 E-02	3.3 E-01	1.6 E+01	5.1 E+01	3.1 E-01
N-Nitrosodiphenylamine	2.6 E-06			9.0 E-03	4.9 E-03	1.8 E+00
p-Nitrosodiphenylamine	6.3 E-06			2.2 E-02		
N-Nitrosodi-n-propylamine	2.0 E-03			7.0 E+00	7.0 E+00	1.0 E+00
N-Nitroso-N-ethylurea	7.7 E-03			2.7 E+01		
N-Nitroso-N-methylethyl-amine	6.3 E-03			2.2 E+01	2.2 E+01	1.0 E+00
N-Nitroso-N-methylurea	3.4 E-02			1.2 E+02		
N-Nitroso-N-methylurethane	3.1 E-02			1.1 E+02		
N-Nitrosomorpholine	1.9 E-03			6.7 E+00		
N-Nitrosonornicotine	4.0 E-04			1.4 E+00		
N-Nitrosopiperidine	2.7 E-03			9.4 E+00		
N-Nitrosopyrrolidine	6.0 E-04	6.1 E-04	9.8 E-01	2.1 E+00	2.1 E+00	1.0 E+00
Pentachlorophenol (PCP)	5.1 E-06			1.8 E-02	1.2 E-01	1.5 E-01
Phenacetin	6.3 E-07			2.2 E-03		
Phenazopyridine	4.9 E-05			1.7 E-01		
Phenazopyridine hydrochloride	4.3 E-05			1.5 E-01		
Phenesterin	4.3 E-02			1.5 E+02		
Phenobarbital	1.3 E-04			4.6 E-01		
Phenoxybenzamine	8.9 E-04			3.1 E+00		
Phenoxybenzamine hydrochloride	7.7 E-04			2.7 E+00		
o-Phenylphenate, sodium	8.6 E-07			3.0 E-03		
Polybrominated biphenyls	8.6 E-03			3.0 E+01	*(8.9 E+00)*	
Polychlorinated biphenyls (PCB)	2.2 E-03			7.7 E+00	7.7 E+00	1.0 E+00
Ponceau MX (D&C Red No.5)	1.3 E-06			4.5 E-03		

Chemical	Inhalation Unit Risk [μg/m^3]$^{-1}$		Ratio of Cal/EPA value to US EPA value	Oral Unit Risk (mg/kg-day)$^{-1}$		Ratio of Cal/EPA value to US EPA value
	Cal/EPA	US EPA [(a)]		Cal/EPA	US EPA [(a)]	
Ponceau 3R (FD&C Red No. 1)	4.6 E-06			1.6 E-02		
Potassium bromate	1.4 E-04			4.9 E-01		
Procarbazine	4.0 E-03			1.4 E+01		
Procarbazine hydrochloride	3.4 E-03			1.2 E+01		
1,3-Propane sultone	6.9 E-04			2.4 E+00		
beta-Propiolactone	4.0 E-03			1.4 E+01		
Propylthiouracil	2.9 E-04			1.0 E+00		
Reserpine	3.1 E-03			1.1 E+01		
Safrole	6.3 E-05			2.2 E-01		
Sterigmatocystin	1.0 E-02			2.2 E-01		
Streptozotocin	3.1 E-02			1.1 E+02		
Styrene oxide	4.6 E-05			1.6 E-01		
Sulfallate	5.4 E-05			1.9 E-01		
2,3,7,8-Tetrachlorodi-benzo-p-dioxin	3.8 E+01	*(3.3 E-05)*		1.3 E+05	*(1.5 E+05)*	
1,1,2,2-Tetrachloroethane	5.8 E-05	5.8 E-05	1.0 E+00	2.7 E-01	2.0 E-01	1.4 E+00
Tetrachloroethylene (PCE, PERC)	5.9 E-06			5.1 E-02		
Thioacetamide	1.7 E-03			6.1 E+00		
4,4'-Thiodianiline	4.3 E-03			1.5 E+01		
Thiourea	2.1 E-05			7.2 E-02		
Toluene diisocyanate	1.1 E-05			3.9 E-02		
ortho-Toluidine	5.1 E-05			1.8 E-01		
ortho-Toluidine hydrochloride	3.7 E-05			1.3 E-01		
Toxaphene	3.4 E-04	3.2 E-04	1.1 E+00	1.2 E+00	1.1 E+00	1.1 E+00
Trichloroethylene (TCE)	2.0 E-06			1.5 E-02		
2,4,6-Trichlorophenol	2.0 E-05	3.1 E-06	6.5 E+00	7.0 E-02	1.1 E-02	6.4 E+00

Chemical	**Inhalation Unit Risk [μg/m^3]$^{-1}$**		**Ratio of Cal/EPA value to US EPA value**	**Oral Unit Risk (mg/kg-day)$^{-1}$**		**Ratio of Cal/EPA value to US EPA value**
	Cal/EPA	**US EPA [(a)]**		**Cal/EPA**	**US EPA [(a)]**	
Tris-(1-aziridinyl)phosphine sulfide (Thiotepa)	3.4 E-03			1.2 E+01		
Tris(2,3-dibromopropyl) phosphate	6.6 E-04			2.3 E+00		
Trp-P-1 (Tryptophan-P-1)	7.4 E-03			2.6 E+01		
Trp-P-2 (Tryptophan-P-2)	9.1 E-04			3.2 E+00		
Urethane (Ethyl carbamate)	2.9 E-04			1.0 E+00		
Vinyl chloride	7.8 E-05	*(3.0 E-01)*		2.7 E-01	*(1.9 E+00)*	
Vinyl trichloride (1,1,2-Trichloroethane)	2.1 E-05	1.6 E-05	1.3 E+00	7.2 E-02	5.7 E-02	1.3 E+00

(a) All US EPA cancer potency values are taken from IRIS (May, 1996) except those in parenthesis; they are taken from HEAST (May, 1995). Cal/EPA values are compared against values listed in IRIS; since only cancer potency values in IRIS represent agency-wide consensus health risk information.

(b) Most of the polyaromatic hydrocarbons listed in the table do not have specific cancer potency factors, but can be assessed using a relative potency scheme with benzo(a)pyrene as the reference compound.

Polyaromatic Hydrocarbon (PAH) or derivative	Suggested PEF
benzo[a]pyrene	1.0 (index compound)
benz[a]anthracene	0.1
benzo[b]fluoranthene	0.1
benzo[j]fluoranthene	0.1
benzo[k]fluoranthene	0.1
dibenz[a,j]acridine	0.1
dibenz[a,h]acridine	0.1
7H-dibenzo[c,g]carbazole	1
dibenzo[a,e]pyrene	1
dibenzo[a,h]pyrene	10
dibenzo[a,i]pyrene	10
dibenzo[a,l]pyrene	10
indeno[1,2,3-c,d]pyrene	0.1
5-methylchrysene	1
1-nitropyrene	0.1
4-nitropyrene	0.1
1,6-dinitropyrene	10
1,8-dinitropyrene	1
6-nitrocrysene	10
2-nitrofluorene	0.01
chrysene	0.01

(c) Cal/EPA inhalation and oral cancer potency values for beryllium sulphate are based on a 1987 US EPA document "Health Assessment Document for Beryllium".

(d) The unit risk of nickel and nickel compounds is developed by Cal/EPA for total nickel; whereas the unit risk developed by US EPA is applicable to nickel refinery dust only.

Attachment B-5

Tabulated Adjustment/Uncertainty Factors Used in the Development of Health-Based Drinking Water Guidance Levels

Chemical	NOAEL (N) or LOAEL (L) (mg/kg-day)	Species	Adverse Effects	Adjustment/ Uncertainty Factors	Daily Water Consumption (l eq./day) [a]	Health-Based Dose (mg/day)	Corresponding Water Concentration (mg/l)
Metals and Inorganic Compounds							
Aluminum	1.8 (N)	human	increased concentration in blood, changes in PO_4 absorption in gastrointestinal tract	10 (most sensitive individual)	2	1.2	0.6
Antimony	0.43 (L)	rat	decreased lifespan, altered level of blood cholesterol and glucose	10 (LOAEL to NOAEL) 10 (animal to human) 10 (most sensitive individual)	2	0.012	0.006
Barium	0.21 (N)	human	cardiovascular effects, hypertension	10 (most sensitive individual)	2	1.2	0.6
Beryllium	0.54 (N)	rat	reduced body weight gain in males from 2 to 6-month of age	10 (possible carcinogen via ingestion) 10 (animal to human) 10 (most sensitive individual)	2	0.008	0.004
Cadmium	0.005 (N)	human	renal dysfunction	10 (most sensitive individual)	2	0.01	0.005
Copper	0.2 (L)	human	gastrointestinal tract irritation	10 (LOAEL to NOAEL) 2 (most sensitive individual)	2	0.4	0.2
Cyanide	10.8 (N)	rat	combined with cytochrome in cells, hypoxia (humans and animals have higher tolerance for cyanide from food than from drinking water)	5 (dietary study) 10 (animal to human) 10 (most sensitive individual)	2	0.3	0.2
Mercury	0.32 (L)	human	kidney damage	10 (LOAEL to NOAEL) 10 (most sensitive individual)	2	0.004	0.002

Chemical	NOAEL (N) or LOAEL (L) (mg/kg-day)	Species	Adverse Effects	Adjustment/ Uncertainty Factors	Daily Water Consumption (l eq./day) [a]	Health-Based Dose (mg/day)	Corresponding Water Concentration (mg/l)
Nickel	5 (N)	rat	decreased body weight, increased relative heart weight, decreased relative liver weight	3 (possible reproductive effects) 10 (animal to human) 10 (most sensitive individual)	2	0.2	0.1
Nitrate as N	1.6 (N)	human	methemoglobinemia	1 (most sensitive individual)	2	20	10
Nitrite as N	1.0 (N)	human	methemoglobinemia	10 (direct toxicity of nitrite)	2	2	1
Total Nitrate and Nitrite	nitrate + nitrite	human	methemoglobinemia	nitrate + nitrite	2	20	10
Selenium	0.04 (L)	human	hair loss, nail changes, skin lesions, nervous system effects	1.5 (LOAEL to NOAEL) 10 (most sensitive individual)	2	0.1	0.05
Thallium	0.25 (N)	rat	blood chemistry changes	3 (lack of chronic and reproductive toxicity data) 10 (subchronic study) 10 (animal to human) 10 (most sensitive individual)	2	0.001	0.0005
Uranium	0.2 (N)	rabbit	kidney toxicity, decreased content of nucleic acids in the renal and hepatic tissues, radiation oncogenic effect	10 (animal to human) 10 (most sensitive individual)	2	0.07	0.035
Organic Compounds							
1,2-Dichloro-benzene (o-DCB)	85.7 (N)	rat, mouse	liver toxicity	10 (subchronic study and lack of reproductive and chronic toxicity in second species) 10 (animal to human) 10 (most sensitive individual)	2	1.2	0.6
1,1-Dichloroethane (1,1-DCA)	273 (L)	rat	increased mortality, decreased body weight gain, clinical signs of intoxication, increased mammary adenocarcinoma, hepatocellular carcinoma, hemangiosarcoma	10 (possible carcinogen) 10 (mortality) 10 (LOAEL to NOAEL) 10 (animal to human) 10 (most sensitive individual)	7	0.01	0.005

Chemical	NOAEL (N) or LOAEL (L) (mg/kg-day)	Species	Adverse Effects	Adjustment/ Uncertainty Factors	Daily Water Consumption (l eq./day) [a]	Health-Based Dose (mg/day)	Corresponding Water Concentration (mg/l)
1,1-Dichloro-ethylene (1,1-DCE,VDC)	9 (L)	rat	hepatic lesions, increased mid-zonal hepatocellular fatty degeneration, kidney toxicity, equivocal evidence of carcinogenicity	10 (possible carcinogen) 10 (LOAEL to NOAEL) 10 (animal to human) 10 (most sensitive individual)	2	0.012	0.006
cis-1,2-Dichloro-ethylene (cis-1,2-DCE)	8.5 (L)	rat	changes in hepatic xenobiotic metabolism, kidney damage	10 (subchronic study) 10 (LOAEL to NOAEL) 10 (animal to human) 10 (most sensitive individual)	2	0.012	0.006
trans-1,2-Dichloro-ethylene (trans-1,2-DCE)	17 (L)	mouse	increased serum glucose level, increased serum alkaline phosphatase in males	10 (subchronic study) 10 (LOAEL to NOAEL) 10 (animal to human) 10 (most sensitive individual)	2	0.02	0.01
Dichloro-difluoro methane (Freon 12)	15 (N)	rat	decreased body weight gain	10 (animal to human) 10 (most sensitive individual)	2	2	1
Ethyl-benzene	97 (N)	rat	increased liver and kidney weights, histopathological changes in liver and kidney	10 (subchronic study) 10 (animal to human) 10 (most sensitive individual)	2	1.3	0.68
Methyl-tert-butyl-ether (MTBE)	50 (L)	rat	anesthetic effect, kidney toxicity	10 (subchronic study) 10 (LOAEL to NOAEL) 10 (animal to human) 10 (most sensitive individual)	2	0.07	0.035
Mono-chloro-benzene (Chloro-benzene)	19.6 (N)	beagle dog	histopathological changes in liver, kidney, gastrointestinal mucosa, mortality, weight loss, changes in hematology and urine analysis	10 (subchronic study) 10 (animal to human) 10 (most sensitive individual)	4	0.14	0.07

Chemical	NOAEL (N) or LOAEL (L) (mg/kg-day)	Species	Adverse Effects	Adjustment/ Uncertainty Factors	Daily Water Consumption (l eq./day) [a]	Health-Based Dose (mg/day)	Corresponding Water Concentration (mg/l)
Styrene	200 (N)	beagle dog	liver toxicity, red blood cell adverse effects	10 (subchronic study) 10 (animal to human) 10 (most sensitive individual)	2	0.2	0.1
1,1,2,2-Tetra-chloroethane (1,1,2,2,-TCA)	1.4 (L)	rat	transient body weight depression, changes in liver fat content	10 (possible carcinogen) 10 (LOAEL to NOAEL) 10 (animal to human) 10 (most sensitive individual)	2	0.002	0.001
Toluene	223 (N)	rat human	decreased liver weight, decreased kidney weight neurotoxicity	10 (LOAEL to NOAEL) 10 (animal to human) 10 (most sensitive individual) 2 (neurotoxicity)	11.2	1.6	0.8
1,2,4-Trichloro-benzene	14.8 (N)	rat	increased adrenal gland weights of the P_0 and F_1 generations associated with histopathological lesion, vacuolization of zona fasciculata in the cortex	10 (use of NOAEL from a less-than-lifetime study) 10 (animal to human) 10 (most sensitive individual)	2	0.14	0.07
1,1,1-Trichloro-ethane (1,1,1-TCA)	3 (N)	rat, mouse	fetal mortality, increased serum enzyme levels, changes in centrilobular hepatocytes	10 (animal to human) 10 (most sensitive individual)	2	0.4	0.2
1,1,2-Trichloroethane (1,1,2-TCA)	3.9 (N)	mouse	altered serum chemistry, systemic tissue damage, liver toxicity, increased hepatocellular carcinoma	10 (possible carcinogen) 10 (use of NOAEL from a less-than-lifetime study) 10 (animal to human) 10 (most sensitive individual)	6.1	0.002	0.001
Trichlorofluoro-methane (Freon 11)	1922 (L)	beagle dog, rat, mouse	mortality, histopathological effect in liver, increased serum urea nitrogen	10 (lack of data on chronic toxicity) 10 (LOAEL to NOAEL) 10 (animal to human) 10 (most sensitive individual)	25.86	0.27	0.15

Chemical	NOAEL (N) or LOAEL (L) (mg/kg-day)	Species	Adverse Effects	Adjustment/ Uncertainty Factors	Daily Water Consumption (l eq./day) [a]	Health-Based Dose (mg/day)	Corresponding Water Concentration (mg/l)
1,1,2-Trichloro-1,2,2-trifluoroethane (Freon 113)	2574 (L)	rat human	increased liver weight psychomotor impairment	10 (LOAEL to NOAEL) 10 (animal to human) 10 (most sensitive individual)	30.2	2.4	1.2
Xylenes (o, p, m)	250 (L)	rat	decreased body weight, increased mortality, hyperactivity in males	10 (LOAEL to NOAEL) 10 (animal to human) 10 (most sensitive individual)	2	3.5	1.75
Pesticides							
Atrazine	0.35 (N)	beagle dog	decreased food intake, body weight, adrenal weight, and hemocrit, occasional tremors and stiffness in the rear limbs, increased mammary tumors in females	10 (possible carcinogen) 10 (animal to human) 10 (most sensitive individual)	2	0.005	0.003
Bentazon	2.5 (N)	beagle dog	decreased body weight, prostatitis, gastrointestinal distress	10 (use of NOAEL from a less-than-lifetime study) 10 (animal to human) 10 (most sensitive individual)	2	0.036	0.018
Carbofuran	0.25 (N)	beagle dog	depressed red blood cell acetylcholinesterase, decreased plasma cholinesterase, testicular degeneration, uterine hyperplasia and hydrometra	10 (animal to human) 10 (most sensitive individual)	2	0.036	0.018
Dalapon	15 (N)	rat	increased kidney-body weight ratio, statistically significant increased body weight in males	3 (incomplete database on chronic toxicity) 10 (animal to human) 10 (most sensitive individual)	2	0.4	0.2

Chemical	NOAEL (N) or LOAEL (L) (mg/kg-day)	Species	Adverse Effects	Adjustment/ Uncertainty Factors	Daily Water Consumption (l eq./day) [(a)]	Health-Based Dose (mg/day)	Corresponding Water Concentration (mg/l)
2,4-Dichlorophenoxy-acetic acid (2,4-D)	1 (N)	rat	blood, liver, and kidney effects	10 (animal to human) 10 (most sensitive individual)	2	0.14	0.07
Di(2-ethyl-hexyl)-adipate (DEHA)	170 (N)	rat, mouse	delayed ossification, reduced reduced maternal body weight, increased parental liver weight, dilated ureters in fetuses, reduced offspring weight gain, reduced litter size, equivocal evidence of carcinogenicity	3 (lack of multi-generation reproductive studies and data in species other than rodents) 10 (possible carcinogen) 10 (animal to human) 10 (most sensitive individual)	2	0.8	0.4
Dinoseb	1 (L)	rat	decreased fetal weight in reproductive toxicity studies	10 (LOAEL to NOAEL) 10 (animal to human) 10 (most sensitive individual)	2	0.014	0.007
Diquat	0.22 (N)	rat	minimal lens opacity, cataract, liver, kidney and gastrointestinal tract damage	10 (animal to human) 10 (most sensitive individual)	2	0.03	0.015
Endothall	2 (N)	dog	increased absolute and relative weights of stomach and small intestine, increased organ-to-body weight ratio	10 (animal to human) 10 (most sensitive individual)	2	0.28	0.1
Endrin	0.025 (N)	dog	mild histological lesions in liver, occasional convulsions	10 (animal to human) 10 (most sensitive individual)	2	0.004	0.002
Glyphosate	10 (N)	rat	systemic toxicity in the F_3 generation, bilateral renal tubular dilatation	10 (animal to human) 10 (most sensitive individual)	2	1.4	0.7
Hexachloro-cyclopenta-diene (HEX)	10 (N)	rat	stomach lesions, mortality	10 (subchronic study) 10 (animal to human) 10 (most sensitive individual)	2	0.1	0.05

Chemical	NOAEL (N) or LOAEL (L) (mg/kg-day)	Species	Adverse Effects	Adjustment/ Uncertainty Factors	Daily Water Consumption (l eq./day) [a]	Health-Based Dose (mg/day)	Corresponding Water Concentration (mg/l)
Methoxychlor	5.01 (N)	rabbit	excessive loss of litters in developmental toxicity studies	10 (poor quality of the critical study and incompleteness of chronic toxicity database) 10 (animal to human) 10 (most sensitive individual)	2	0.08	0.04
Molinate (Ordam)	0.2 (N)	rat	decreased number of female pups, increased body weight of pups, decreased number of viable fetuses per litter	10 (animal to human) 10 (most sensitive individual)	2	0.04	0.02
Oxamyl (Vydate)	2.5 (N)	rat	decreased body weight gain and food consumption	10 (animal to human) 10 (most sensitive individual)	2	0.4	0.2
Picloram	7 (N)	dog	increased liver weight, reduced food consumption and body weight, elevated serum alkaline phosphatase	10 (animal to human) 10 (most sensitive individual)	2	1	0.5
Simazine	0.5 (N)	rat	weight changes, hematologic effects in females, increased mammary carcinoma in females	10 (possible carcinogen) 10 (animal to human) 10 (most sensitive individual)	2	0.007	0.004

Chemical	NOAEL (N) or LOAEL (L) (mg/kg-day)	Species	Adverse Effects	Adjustment/ Uncertainty Factors	Daily Water Consumption (l eq./day) [a]	Health-Based Dose (mg/day)	Corresponding Water Concentration (mg/l)
Thio-bencarb (Bolero)	1 (N)	rat	decreased body weight gain, decreased food consumption, hair loss and scabs, sores on hind feet, decreased urine volume, hematological changes (increased red blood cell volume, red blood cell counts, hemoglobin concentration)	10 (animal to human) 10 (most sensitive individual)	2	0.14	0.07
		beagle dog	decreased plasma cholinesterase, changes in serum chemistry (increased alkaline phosphatase, increased cholesterol, decreased alanine aminotransferase, decreased serum albumin), increased neutrophile, decreased red blood cell				
2(2,4,5-Tri-chloro-phenoxy)-propionic acid (Silvex,2,4,5-TP)	0.75 (N)	dog	histopathological changes in liver, renal toxicity	10 (animal to human) 10 (most sensitive individual)	2	0.1	0.05

(a) Equivalent liters of water consumed per day. This is to account for other exposure routes besides drinking water consumption. For example, inhalation and dermal exposure to volatile organic compounds in bathing or showering water are considered where appropriate.

Note: Relative source contribution of all the listed chemicals is assumed to be 0.2 with the exception of the following 6 elements:

Aluminum	0.1
Antimony	0.4
Barium	0.83
Cadmium	0.25
Copper	1
Uranium	0.5