

APPENDIX 8.5 DERIVATION OF TOXICITY REFERENCE DOSE FOR MARINE MAMMALS

Toxicological effects data were reviewed from various scientific literature, database and guidelines, including toxicological profiles of ATSDR, Sample *et al.* (1996), IRIS Database, WHO (2000) and NHMRC (2004). As toxicological data are not available specifically for dolphins or porpoises, it was necessary to use toxicological data for surrogate species. The toxicological data reviewed were summarized at the end of this Appendix.

The following rules are adopted to derive COC-specific toxicity reference dose (equivalent to a chronic No Observable Adverse Effect Level (NOAEL)) for marine mammals from the toxicological data reviewed, based on the hierarchy described in SSDS/EIAS DRA (1998):

- Rule 1: Toxicity data shall be ecologically relevant to the Study
 - Ecological endpoint: ecologically relevant endpoint such as reproduction, development and survival (desired endpoint) shall be used when available
- Rule 2: For exposure duration, chronic exposure is preferred to subchronic exposure; subchronic exposure is preferred to acute exposure
- Rule 3: The following framework shall be followed for selection of study endpoint:
 - If highest reported NOAEL is below all available LOAELs (Lowest Observed Adverse Effect Level) across all species for the desired endpoints → the highest NOAEL is selected
 - If a LOAEL for a test species is same to or below the highest NOAEL (either from the same test species or another species) → the highest NOAEL is not selected; the highest NOAEL which falls below the lowest LOAEL is selected
 - If the lowest NOAEL is greater than the lowest LOAEL (of a different study) → the lowest available LOAEL is selected
 - If only one NOAEL and LOAEL are available → the lowest of the two values is selected
- Rule 4: UF shall be applied to convert a toxicity endpoint (not a chronic NOAEL) to a chronic NOAEL (adopted from USEPA (1999b)):
 - Chronic LOAEL should be multiplied by a UF of 0.1
 - Subchronic NOAEL should be multiplied by a UF of 0.1
 - Acute lethal value (such as LD50) should be multiplied by an UF of 0.01
- Rule 5: UF shall be applied to extrapolate a NOAEL for one type of organism to another:
 - NOAEL = NOAEL of organism in different family but same order x 0.5
 - NOAEL = NOAEL of organism in different order but same class x 0.5
 - NOAEL = NOAEL of organism which is non-protected species x 0.5

The derived toxicity reference doses are presented in **Table 1**.

Table 1 Toxicity Reference Doses

COC	Toxicological Data Adopted (mg/kg/d)	UF Used	Toxicity Reference Dose Derived (mg/kg/d)
Bromoform	100, chronic NOAEL (reproductive effect) for mouse	$0.5 \times 0.5 \times 0.5 = 0.125$	12.5
Chloroform	30, chronic NOAEL (reproductive effect) for dog	$0.5 \times 0.5 \times 0.5 = 0.125$	3.75
Dibromochloromethane	80, chronic NOAEL (reproductive effect) for rat	$0.5 \times 0.5 \times 0.5 = 0.125$	10.0
Dibromoacetic acid	2, subchronic NOAEL (reproductive effect) for rat	$0.5 \times 0.5 \times 0.5 \times 0.1 = 0.0125$	0.025
Chloroacetic acid	15, chronic LOAEL (decreased survival) for rat	$0.5 \times 0.5 \times 0.5 \times 0.1 = 0.0125$	0.1875

COC	Toxicological Data Adopted (mg/kg/d)	UF Used	Toxicity Reference Dose Derived (mg/kg/d)
Dichloroacetic acid	7.6, subchronic NOAEL for mice	$0.5 \times 0.5 \times 0.5 \times 0.1 = 0.0125$	0.095
Trichloroacetic acid	36, subchronic NOAEL for rat	$0.5 \times 0.5 \times 0.5 \times 0.1 = 0.0125$	0.45
Total residual chlorine	15, chronic NOAEL for rats and mice	$0.5 \times 0.5 \times 0.5 = 0.125$	1.875
Tetrachloroethylene	386, chronic LOAEL for mouse	$0.5 \times 0.5 \times 0.5 \times 0.1 = 0.0125$	4.825
Trichloroethylene	500, chronic LOAEL for rat	$0.5 \times 0.5 \times 0.5 \times 0.1 = 0.0125$	6.25
2,4,6-trichlorophenol	1300, chronic NOAEL for mouse	$0.5 \times 0.5 \times 0.5 = 0.125$	162.5
Hexachlorobenzene	11, chronic LOAEL for dog	$0.5 \times 0.5 \times 0.5 \times 0.1 = 0.0125$	0.1375
Beta-BHC	0.2, chronic NOAEL for rat	$0.5 \times 0.5 \times 0.5 = 0.125$	0.025
Gamma-BHC	32, chronic LOAEL for rat	$0.5 \times 0.5 \times 0.5 \times 0.1 = 0.0125$	0.4
Aluminum	49, chronic NOAEL for mouse	$0.5 \times 0.5 \times 0.5 \times 0.1 = 0.125$	6.125
Antimony	1.25, chronic LOAEL for mouse	$0.5 \times 0.5 \times 0.5 \times 0.1 = 0.0125$	0.015625
Barium	15, chronic NOAEL for rat	$0.5 \times 0.5 \times 0.5 = 0.125$	1.875
Chromium (III)	2,737, chronic NOAEL for rat	$0.5 \times 0.5 \times 0.5 = 0.125$	342.125
Copper	12, chronic NOAEL for mink	$0.5 \times 0.5 \times 0.5 = 0.125$	1.5
Lead	8, chronic NOAEL for rat	$0.5 \times 0.5 \times 0.5 = 0.125$	1
Nickel	40, chronic NOAEL for rat	$0.5 \times 0.5 \times 0.5 = 0.125$	5
Selenium	0.21, chronic NOAEL for rat	$0.5 \times 0.5 \times 0.5 = 0.125$	0.02625
Silver	222.2, chronic LOAEL for rat	$0.5 \times 0.5 \times 0.5 \times 0.1 = 0.0125$	2.7775
Tin	23.4, chronic NOAEL for mouse	$0.5 \times 0.5 \times 0.5 = 0.125$	2.925
Vanadium	2.1, chronic LOAEL for rat	$0.5 \times 0.5 \times 0.5 \times 0.1 = 0.0125$	0.02625
Zinc	160, chronic NOAEL for rat	$0.5 \times 0.5 \times 0.5 = 0.125$	20
Ammonia	412, subchronic NOAEL for rat	$0.5 \times 0.5 \times 0.5 \times 0.1 = 0.0125$	5.15
Dioxins and furans (TEQ)	7.1E-5, chronic NOAEL for rat	$0.5 \times 0.5 \times 0.5 = 0.125$	8.875E-6
Toluene	260, chronic LOAEL for mouse	$0.5 \times 0.5 \times 0.5 \times 0.1 = 0.0125$	3.25
Diazinon	12, chronic NOAEL for rat	$0.5 \times 0.5 \times 0.5 = 0.125$	1.5
Malathion	359, chronic LOAEL for rat	$0.5 \times 0.5 \times 0.5 \times 0.1 = 0.0125$	4.4875

Toxicological Data of COCs Reviewed

	NOAEL (mg/kg/d)	LOAEL (mg/kg/d)	Source
Bromoform			
Rat (Fischer-344) male 103wk, 5d/wk (chronic)		200 (decreased survival)	ATSDR
Rat (Fischer-344) male 103wk, 5d/wk (chronic)	100 (reproductive)	200 (reproductive)	
Rat (Fischer-344) female 103wk, 5d/wk (chronic)	200 (reproductive)		
Mouse (B6C3F1) male 103wk, 5d/wk (chronic)	100 (reproductive)		
Mouse (B6C3F1) female 103wk, 5d/wk (chronic)	200 (reproductive)		
Rat, subchronic oral gavage bioassay	17.9 (hepatic lesions)	35.7 (hepatic lesions)	IRIS
Rat, 13 weeks oral gavage bioassay (subchronic)	25 (hepatic lesions)		WHO EHC 216
Chloroform			
Rat (Osborne-Mendel), male 78wk, 5d/wk, 1 time/d (chronic)	180 (reproductive)	90 (decreased survival)	ATSDR
Rat (Osborne-Mendel), female 78wk, 5d/wk, 1 time/d (chronic)	200 (reproductive)	100 (decreased survival)	
Mouse (B6C3F1), female 78wk, 5d/wk, 1 time/d (chronic)	477 (reproductive)	477 (decreased survival)	
Mouse (B6C3F1), male 78wk, 5d/wk, 1 time/d (chronic)	277 (reproductive)		
Dog (Beagle) 7.5yr, 6d/wk (chronic)	30 (reproductive)		
Dog Chronic oral bioassay		12.9 (moderate/marked fatty cyst formation in the liver and elevated SGPT)	IRIS
Mice 3 weeks, administration in corn oil (subchronic)	10 (cytolethality and regenerative hyperplasia)		WHO EHC 216
Rat 13 wk (subchronic)	15 (liver, kidney gonad condition)	41 (liver, kidney gonad condition)	ORNL
Dibromochloromethane			
Mouse (B6C3F1) 105wk, 5d/wk (chronic)		100 (decreased survival)	ATSDR
Rat (Fischer-344) 2yr, 5d/wk (chronic)	80 (reproductive)		
Mouse (B6C3F1) 105wk, 5d/wk (chronic)	100 (reproductive)		
Rat Subchronic gavage bioassay	21.4 (hepatic lesions)	42.9 (hepatic lesions)	IRIS
Rat 13 week corn oil gavage (subchronic)	30 (hisopathological effect)		WHO EHC 216

	NOAEL (mg/kg/d)	LOAEL (mg/kg/d)	Source
Dibromoacetic acid			
Rat, male 79 days (subchronic)	2 (reproductive)		WHO EHC 216
Chloroacetic acid			
Rat 2-year (chronic)		15 (decreased survival)	NHMRC
Dichloroacetic acid			
Mice 90-day (subchronic)	7.6		NHMRC
Dog Subchronic oral		12.5 (lesions in the testes, cerebrum, cerebellum, and liver)	IRIS
Mice 8 weeks (subchronic)	40 (hepatomegaly and glycogen accumulation)	100 (hepatomegaly and glycogen accumulation)	WHO EHC 216
Trichloroacetic acid			
Rat, male 90-day (subchronic)	36		NHMRC
Mice Long-term study	40 (hepatic toxicity)		WHO EHC 216
Total residual chlorine			
Rat Chronic drinking water study	14.4		IRIS
Rats and mice 2-year drinking water study (chronic)	15		NHMRC, WHO EHC 216
Tetrachloroethylene			
Rat (Subchronic test)	14 (hepatotoxicity)		IRIS
Rat (Subchronic test)	14		NHMRC
Rat, male (Chronic test)		471 (decreased survival)	ATSDR
Rat, female (Chronic test)		474 (decreased survival)	
Mouse, female (Chronic test)		386 (reduced survival)	
Mouse, male (Chronic test)		536 (reduced survival)	
Rat (Chronic test)	941 (systematic effect)		
Rat, male (Chronic test)		471 (renal nephropathy)	
Rat, female (Chronic test)		474 (renal nephropathy)	
Mouse (Chronic test)	1,072 (systematic effect)		
Mouse, female (Chronic test)		386 (renal nephropathy)	
Mouse, male (Chronic test)		536 (renal nephropathy)	
Mouse (Subchronic test)	1.4 (hepatotoxicity)	7 (hepatotoxicity)	ORNL

	NOAEL (mg/kg/d)	LOAEL (mg/kg/d)	Source
Trichloroethylene			
Mouse (Subchronic test)		100 (minor effect on relative liver weight)	IRIS
Rat, male (Chronic test)		1,097 (decreased survival)	ATSDR
Rat, female (Chronic test)		549 (decreased survival)	
Rat, male (Chronic test)		500 (decreased survival)	
Rat, female (Chronic test)		500 (decreased survival)	
Mouse, female (Chronic test)		869 (decreased survival)	
Mouse, male (Chronic test)		1,000 (decreased survival)	
Rat (Chronic test)	250 (systematic effect)		
Rat, male (Chronic test)	50 (renal effect)	250 (renal effect)	
Rat (Chronic test)	1,097 (systematic effect)		
Rat (Chronic test)		549 (toxic nephrosis, proximal tubular epithelium alterations)	
Rat (Chronic test)		549 (alopecia, roughening of hair coat, sores)	
Rat (Chronic test)		549 (squinting, red discharge)	
Rat, male (Chronic test)	549 (body weight decreased)	1,097 (body weight decreased)	
Rat, female (Chronic test)		549 (body weight decreased)	
Rat (Chronic test)	1,000 (systematic effect)		
Rat (Chronic test)		500 (toxic nephrosis, cytomegaly)	
Rat, male (Chronic test)		500 (body weight decreased)	
Rat (Chronic test)	1,000 (systematic effect)		
Rat (Chronic test)		500 (toxic nephrosis, cytomegaly)	
Rat, male (Chronic test)	500 (body weight decreased)	1,000 (body weight decreased)	
Mouse, male (Chronic test)	2,239 (systematic effect)	1,160 (toxic nephrosis)	
Mouse, female (Chronic test)		569 (alopecia, skin sores)	
Mouse (Chronic test)	1,000 (systematic effect)	1,000 (alight to moderate toxic nephrosis, cytomegaly)	
Mouse, male (Chronic test)		1,000 (decreased body weight)	
Mouse (Subchronic test)	0.7 (hepatotoxicity)	7 (hepatotoxicity)	ORNL

	NOAEL (mg/kg/d)	LOAEL (mg/kg/d)	Source
2,4,6-trichlorophenol			
Rat (Chronic test)	4.5		NHMRC
Rat (Chronic effect)	500 (systematic effect)	250 (bone marrow hyperplasia)	ATSDR
Rat, female (Chronic effect)		500 (decreased body weight)	
Mouse, male (Chronic effect)	1,300 (systematic effect)	650 (hepatic hyperplasia)	
Mouse (Chronic effect)	1,356 (systematic effect)		
Mouse, female (Chronic effect)		658 (reduced body weight)	
Rat (Chronic test)	500 (immuno / lymphor effect)		
Rat (Chronic effect)	500 (neurological effect)		
Mouse, female (Chronic test)	1,356 (neurological effect)		
Rat (Chronic test)	500 (reproductive)		
Mouse, male (Chronic test)	1,300 (reproductive)		
Mouse, female (Chronic test)	1,356 (reproductive)		
Hexachlorobenzene			
Rat (Chronic test)	0.08 (liver effect)		IRIS
Mouse (Chronic test)		24 (decreased survival)	ATSDR
Dog, female (Chronic test)		11 (decrease survival)	
Rat (Chronic test)	0.05 (hepatic effect)	0.25 (mitochondrial swelling and elongation)	
Rat, female (Chronic test)		7 (systematic effect)	
Rat (Chronic test)		10 (systematic effect)	
Rat, female (Chronic effect)		10 (hepatic effect)	
Rat, female (Chronic effect)	10 (decreased body weight)		
Mouse, male (Chronic test)		13 (hepatic effect)	
Hamster, male (Chronic test)		16 (decreased in weight gain)	
Dog (Chronic test)	11 (Cardiovascular system)	110 (arteriopathy)	
Dog (Chronic test)	1 (Gastro effect)	11 (diarrhea, necrotic and inflammatory lesions of the omentum and abdominal serosa)	
Dog (Chronic test)	1 (hemato effect)	110 (anemia)	

	NOAEL (mg/kg/d)	LOAEL (mg/kg/d)	Source
Hexachlorobenzene (Con't)			
Dog (Chronic test)	1 (hepatic effect)	11 (hepatomegaly, bile duct hyperplasia, pericholangitis, periportal fibrosis)	
Dog (Chronic test)	1 (decreased body weight)	11 (decreased body weight)	
Dog (Chronic test)		0.1 (immuno / lymphoret effect)	
Mouse (Chronic test)		24 (tremors, convulsions)	
b-BHC			
Rat, female (Chronic test)	5 (hemato effect)		ATSDR
Rat, male (Chronic test)		22.5 (decreased red blood cells, leukocyte and hemoglobin concentrations)	
Rat, male (Chronic test)		4.5 (hyalinization of centrilobular cells)	
Rat, male (Chronic test)	4.5 (renal effect)	22.5 (calcinosis)	
Rat, female (Chronic test)	5 (decreased in body weight)		
Mouse, female (Chronic test)	20 (hepatic effect)		
Mouse, male (Chronic test)		54 (nuclear irregularities in foci of enlarged hepatocytes)	
Mouse, male (Chronic test)		45 (centrilobular hypertrophy)	
Rat, female (Chronic test)	5 (immuno / lymphoret effect)		
Rat, male (Chronic test)		22.5 (cortical atrophy in thymus)	
Rat, female (Chronic test)	5 (neurological effect)		
Rat, male (Chronic test)		22.5 (ataxia, coma)	
Rat, male (Chronic test)	0.9 (reproductive)	22.5 (atrophy of testes)	
Rat, female (Chronic test)	0.2 (reproductive)	25 (atrophy of ovary)	

	NOAEL (mg/kg/d)	LOAEL (mg/kg/d)	Source
g-BHC			
Rat, female (Chronic test)		32 (increased mortality rate)	ATSDR
Rat, male (Chronic test)		7 (hepatic effect)	
Rat, female (Chronic test)	32 (renal effect)		
Rat, female (Chronic test)	4 (systematic effect)		
Rat, male (Chronic test)		112 (moderate microscopic damage of hepatic cell)	
Rat, female (Chronic test)	64 (decreased body weight gain)		
Rat, male (Chronic test)		112 (decreased body weight gain)	
Rat (Chronic test)	9 (hepatic effect)		
Rat (Chronic test)	8 (reproductive effect)		ORNL
Antimony			
Rat (Chronic test)		0.35 (longevity, blood glucose, and cholesterol)	IRIS
Rat (Chronic test)	6 (decreased body weight gain and reduced food and water intake)		WHO (2004)
Rat (Chronic test)		0.262 (decreased lifespan)	ATSDR
Mouse, female (Chronic test)		0.35 (decreased lifespan)	
Rat (Chronic test)	0.262 (cardio effect)	0.262 (decreased nonfasting serum glucose, increased serum cholesterol)	
Mouse (Chronic test)	0.35 (hepatic effect)		
Mouse (Chronic test)		1.25 (longevity)	ORNL

	NOAEL (mg/kg/d)	LOAEL (mg/kg/d)	Source
Barium			
Mouse, male (Chronic test)		160 (increased mortality)	ATSDR
Rat, male (Chronic test)	15 (systematic effect)		
Rat (Chronic test)	60 (systematic effect)		
Rat, female (Chronic test)	0.17 (cardio effect)	7.2 (depressed rates of cardiac contraction and electrical conductivity)	
Rat, female (Chronic test)		0.8 (increased blood pressure)	
Mouse, male (Chronic test)	160 (systematic effect)		
Mouse, male (Chronic test)	75 (renal effect)	160 (marked nephropathy)	
Mouse, male (Chronic test)	75 (body weight)	160 (weight loss)	
Rat, male (Chronic test)	15 (immuno/lymphoret effect)		
Rat, male (Chronic test)	60 (immuno/lymphoret effect)		
Mouse, male (Chronic test)	75 (immuno/lymphoret effect)	160 (lymphoid depletion in the spleen and decreased relative and absolute spleen weight)	
Rat, male (Chronic test)	15 (immuno/lymphoret effect)		
Rat, male (Chronic test)	60 (immuno/lymphoret effect)		
Mouse, male (Chronic test)	160 (immuno/lymphoret effect)		
Rat, male (Chronic test)	15 (reproductive effect)		
Rat, male (Chronic test)	60 (reproductive effect)		
Rat, female (Chronic test)	75 (reproductive effect)		
Mouse, male (Chronic test)	160 (reproductive effect)		
Mouse, female (Chronic test)	200 (reproductive effect)		
Rat (Chronic test)	5.1 (growth)		
Rat (Chronic test)		19.8 (mortality)	

	NOAEL (mg/kg/d)	LOAEL (mg/kg/d)	Source	
Chromium				
Rat (Chronic test)	1,468		IRIS	
Rat (Chronic test)	2,040 (systematic effect)		ATSDR	
Rat (Chronic test)	3.6 (systematic effect)			
Rat (Chronic test)	0.46 (systematic effect)			
Rat (Chronic test)	2,737 (longevity)		ORNL	
Copper				
Mouse, male (Chronic test)	42 (decrease in body weight)		ATSDR	
Rat, male (Subchronic test)	66 (reproductive effect)			
Rat, female (Subchronic test)	68 (reproductive effect)			
Mink (Subchronic test)	12 (reproductive effect)			
Mink (Chronic test)	11.7 (reproductive effect)	15.14 (reproductive effect)	ORNL	
Lead				
Rat (Chronic test)	8 (reproductive effect)	80 (reproductive effect)	ORNL	
Nickel				
Rat (Chronic test)	5 (decreased body and organ weights)		IRIS, WHO (2004)	
Rat (Chronic test)	187.5 (systematic effect)		ATSDR	
Rat (Chronic test)	7.5 (decrease in body weight)	187.5 (decreased body weight gain)		
Dog (Chronic test)	25 (respiratory effect)	62.5 (cholesterol granulomas, emphysema, bronchiolectasis)		
Dog (Chronic test)	62.5 (systematic effect)			
Dog (Chronic test)	25 (hemato effect)	62.5 (decreased hemaocrit and hemoglobin levels)		
Dog (Chronic test)	25 (renal effect)	62.5 (increased kidney weight)		
Dog (Chronic test)	25 (decreased in body weight gain)	62.5 (decreased in body weight gain)		
Rat (Chronic test)	187.5 (immuno/lymphoret effect)			
Dog (Chronic test)	62.5 (immuno/lymphoret effect)			
Rat (Chronic test)	187.5 (neurological effect)			
Dog (Chronic test)	62.5 (neurological effect)			
Rat (Chronic test)	40 (reproductive effect)	80 (reproductive effect)		ORNL

	NOAEL (mg/kg/d)	LOAEL (mg/kg/d)	Source
Selenium			
Rat (Chronic test)		0.5 (reduced longevity)	ATSDR
Rat (Chronic test)	0.1 (muscular/skeletal effect)	0.2 (soft bones)	
Rat (Chronic test)	0.025 (hepatic effect)	0.1 (hyperplastic lesions)	
Rat (Chronic test)	0.025 (renal effect)	0.1 (nephritis)	
Rat, female (Chronic test)	0.5 (systematic effect)		
Rat, female (Chronic test)		0.25 (slight to moderate cirrhosis)	
Mouse (Chronic test)		0.57 (amyloidosis)	
Mouse (Chronic test)	0.57 (decrease in body weight)		
Rat (Chronic test)	0.21 (reproductive effect)	1.05 (decreased fertility, maternal toxicity)	
Rat (Chronic test)	0.20 (reproductive effect)	0.33 (reproductive effect)	ORNL
Silver			
Rat (Subchronic test)		222.2 (decreased weight gain)	ATSDR
Mouse (Subchronic test)		18.1 (hypoactivity)	
Tin			
Rat (Chronic test)	63 (systematic effect)		ATSDR
Rat (Chronic test)		0.7 (systematic effect)	
Mouse (Chronic test)	164 (systematic effect)		
Mouse (Chronic test)	0.7 (decrease in body weight)		
Mouse (Chronic test)	23.4 (reproductive effect)	35 (reproductive effect)	ORNL
Vanadium			
Rat (Chronic test)	0.89 (decreased hair cystine)		IRIS
Rat (Chronic test)	0.7 (systematic effect)		ATSDR
Mouse (Chronic test)	4.1 (systematic effect)		
Mouse (Chronic test)	0.54 (other effect)		
Rat (Chronic test)		2.1 (reproductive effect)	ORNL
Zinc			
Rat (Chronic test)	160 (reproductive effect)	320 (reproductive effect)	ORNL

	NOAEL (mg/kg/d)	LOAEL (mg/kg/d)	Source
Ammonia			
Rat, female (Subchronic test)	22 (decrease body weight)	3,150 (reduction in body weight)	ATSDR
Rat (Subchronic test)	22 (decrease body weight)	3,102.2 (reduced body weight gain)	
Rat (Subchronic test)	412 (renal effect)		
Rat, female (Subchronic test)	79 (systematic effect)		
Dog (Subchronic test)		337 (bone deformity and softening)	
Rat (Subchronic test)	22 (neurological effect)	3,102.2 (decreased binding of somatostatin to receptors in frontoparietal cortex and hippocampus)	
Rat (Subchronic test)		4,293 (decreased body weight)	
	NOAEL (µg/kg/d)	LOAEL (µg/kg/d)	Source
Dioxins and Furans			
Rat (Chronic test)		0.1 (increased mortality)	ATSDR
Mouse (Chronic test)		0.36 (increased mortality)	
Mouse, male (Chronic test)		1 (decreased survival)	
Rat (Chronic test)	0.01 (respiratory effect)	0.1 (local alveolar hyperplasia)	
Rat (Chronic test)	0.01 (cardio effect)	0.1 (myocardial degeneration, periarteritis)	
Rat (Chronic test)	0.1 (gastro effect)		
Rat (Chronic test)	0.01 (hemato effect)	0.1 (decreased erythrocytes)	
Rat (Chronic test)	0.1 (muscular/skeletal effect)		
Rat (Chronic test)		0.01 (severe and extensive hepatic necrosis)	
Rat (Chronic test)	0.1 (renal effect)		
Rat (Chronic test)		0.1 (decreased in body weight gain)	
Rat (Chronic test)	0.071 (systematic effect)		
Rat (Chronic test)	0.0071 (hepatic effect)	0.071 (toxic hepatitis)	
Rat (Chronic test)		0.0014 (decrease in body weight gain)	

	NOAEL (µg/kg/d)	LOAEL (µg/kg/d)	Source
Dioxins and Furans (Con't)			
Rat (Chronic test)	0.286 (systematic effect)		ATSDR
Rat (Chronic test)	0.057 (decrease in weight gain)		
Rat, male (Chronic test)		0.0286 (decreased weight gain)	
Mouse (Chronic test)		0.36 (dermatitis)	
Mouse (Chronic test)		0.36 (decreased weight gain)	
Mouse (Chronic test)	0.3 (systematic effect)		
Mouse (Chronic test)	0.0071 (renal effect)	0.071 (lymphocytic inflammatory infiltration in kidney)	
Monkey (Chronic test)	0.001 (immuno/lymphoret effect)		
Rat (Chronic test)	0.01 (immuno/lymphoret effect)	0.1 (thymic atrophy)	
Rat (Chronic test)	0.071 (immuno/lymphoret effect)		ATSDR
Rat, male (Chronic test)	0.286 (immuno/lymphoret effect)		
Mouse (Chronic test)	0.3 (immuno/lymphoret effect)		
Mouse, female (Chronic test)		0.03 (decrease in the effector and memory T cell phenotypes)	
Rat (Chronic test)	0.01 (neurological effect)	0.1 (hemorrhage in brain)	
Rat (Chronic test)	0.071 (neurological effect)		
Mouse (Chronic test)	0.3 (neurological effect)		
Rat (Chronic test)	0.1 (reproductive effect)		
Rat (Chronic test)	0.071 (reproductive effect)		
Mouse (Chronic test)	0.3 (reproductive effect)		

	NOAEL (mg/kg/d)	LOAEL (mg/kg/d)	Source
Toluene			
Mouse (Chronic test)		260 (reproductive effect)	ORNL
Diazinon			
Rat, male (Chronic test)	10 (systematic effect)		ATSDR
Rat, female (Chronic test)	12 (systematic effect)		
Rat, male (Chronic test)	10 (immuno/lymphoret effect)		
Rat, female (Chronic test)	12 (immuno/lymphoret effect)		
Rat, male (Chronic test)	0.06 (neurological effect)	5 (decrease in brain AChE)	
Rat, female (Chronic test)	0.07 (neurological effect)	6 (decrease in brain AChE)	
Rat, male (Chronic test)	10 (reproductive effect)		
Rat, female (Chronic test)	12 (reproductive effect)		

	NOAEL (mg/kg/d)	LOAEL (mg/kg/d)	Source
Malathion			
Rat, male (Chronic test)		359 (significant increase in deaths)	ATSDR
Rat, male (Chronic test)		166 (increased mortality)	
Rat, female (Chronic test)	35 (systematic effect)	415 (increased absolute and relative thyroid and parathyroid weight)	
Rat, male (Chronic test)		359 (systematic effect)	
Rat (Chronic test)	332 (systematic effect)		
Rat, male (Chronic test)		166 (chronic inflammation of the stomach and stomach ulcers)	
Rat, female (Chronic test)		166 (fatty metamorphosis of the liver)	
Mouse (Chronic test)	2,980 (systematic effect)		
Mouse, male (Chronic test)	17.4 (respiratory effect)	1,476 (systematic effect)	
Mouse, female (Chronic test)	167 (systematic effect)		
Rat, male (Chronic test)	2 (neurological effect)	359 (inhibition of plasma cholinesterase)	
Mouse, female (Chronic test)	20.8 (neurological effect)		
Mouse, male (Chronic test)		1,476 (inhibition of plasma and RBC cholinesterase activity)	
Mouse (Chronic test)		1,490 (cystic endometrial hyperplasia)	

Note: Bolded value was used to derive toxicological reference dose