Table 3-1 Levels of Significant Exposure to Cadmium - Inhalation

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/m³)	LOAEL Less Serious (mg/m³)	LOAEL Serious (mg/m³)	Reference Chemical Form	Comments
ACUTE EXPOSURE								
Death								
1	Human	5 hr (occup)				8.63 M (5 male workers died after a 5 hour exposure)	Beton et al. 1966 CdO fume	
2	Rat (NS)	10-15 min				30 (LC50 at 7 days)	Barrett et al. 1947 CdO fume	
3	Rat (Fischer- 344)	6.2 hr/d 5 d/wk 2 wk				8.8 (100% mortality by day 6)	NTP 1995 CdO	
4	Rat (Sprague-Dawley)	2 hr				112 (25/32 died within 1 week)	Rusch et al. 1986 CdO fume	
5	Rat (Sprague-Dawley)	3 d 1 hr/d				61 M (17/18 died within 3 days)	Snider et al. 1973 CdCl2	
6	Mouse (B6C3F1)	6.2 hr/d 5 d/wk 2 wk				8.8 (100% mortality by day 7)	NTP 1995 CdO	
7	Rabbit (NS)	4 hr				28.4 (LC50 at 14 days)	Friberg 1950 Cd metal dust	

Table 3-1 Levels of Significant Exposure to Cadmium - Inhalation (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/m³)	LOAEL Less Serious (mg/m³)	LOAEL Serious (mg/m³)	Reference Chemical Form	Comments
Systemic								
8	Rat (Long- Evans)	1 hr	Resp			5 M (pulmonary edema, enzyme changes associated with type 2 cell hyperplasia)	Boudreau et al. 1989 CdCl2	
9	Rat (Wistar)	3 hr	Resp		0.4 M (mild hypercellularity at the bronchoalveolar junction and in adjacent alveoli)	4.6 M (persistent focal interstitial thickening, increased collagen, general hypercellularity)	Buckley and Bassett 1987b CdO dust	
			Bd Wt	0.4 M	4.6 M (15% decreased body weight)			
10	Rat (Sprague-Dawley)	1 hr	Resp			6.5 M (severe pneumonitis)	Bus et al. 1978 CdCl2	
			Bd Wt		6.5 M (10.8% decreased body weight)			
11	Rat (Sprague-Dawley)	2 hr	Resp	0.45 M		4.5 M (moderate to severe pneumonitis, hemorrhage, edema)	Grose et al. 1987 CdCl2	
			Bd Wt			4.5 M (20% decreased body weight)		

Table 3-1 Levels of Significant Exposure to Cadmium - Inhalation (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/m³)	LOAEL Less Serious (mg/m³)	LOAEL Serious (mg/m³)	Reference Chemical Form	Comments
12	Rat (Sprague-Dawley)	2 hr	Resp		0.45 M (significant increased absolute and relative lung weight)	4.5 M (severe pneumonitis, hyperplasia of type 2 cells and fibroblasts)	Grose et al. 1987 CdO dust	
			Bd Wt	0.45 M				
13	Rat (Lewis)	1-6 wk 5 d/wk 3 hr/d	Resp			1.6 M (interstitial pneumonitis)	Hart 1986 CdO dust	
14	Rat (Wistar)	10 d 6 hr/d	Bd Wt	0.17 M			Klimisch 1993 CdCl2	No histopathological examination.
15	Rat (Wistar)	10 d 6 hr/d	Bd Wt	6.29 M			Klimisch 1993 CdS	No histopathological examination.
16	Rat (Fischer- 344)	6.2 hr/d 5 d/wk 2 wk	Resp		0.88 F (degeneration of nasal olfactory epithelium)	8.8 (marked necrosis of alveolar ducts)	NTP 1995 CdO	
					0.088[b] (alveolar histiocytic infiltrate and focal inflammation in alveolar septa)			
			Hepatic	2.6				
			Renal	2.6				

Table 3-1 Levels of Significant Exposure to Cadmium - Inhalation (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/m³)	LOAEL Less Serious (mg/m³)	LOAEL Serious (mg/m³)	Reference Chemical Form	Comments
17	Rat (Sprague-Dawley)	2 hr	Resp			6 M (alveolar type 1 cell damage and necrosis)	Palmer et al. 1986 CdCl2	
			Endocr	6 M				
			Bd Wt	6 M				
18	Rat (Sprague-Dawley)	2 hr	Gastro		132 (erosions of the stomach)		Rusch et al. 1986 CdCO3	
19	Rat (Sprague-Dawley)	5, 10, or 15 d 1 hr/d	Resp			6.1 M (emphysema)	Snider et al. 1973 CdCl2	
20	Rat (Sprague-Dawley)	3 d 1 hr/d	Resp			61 M (pulmonary hemorrhage)	Snider et al. 1973 CdCl2	
21	Mouse (B6C3F1)	6.2 hr/d 5 d/wk 2 wk	Resp		0.88 (fibrosis and inflammation around the alveolar ducts, necrosis of the alveolar duct epithelium)		NTP 1995 CdO	
					0.088 (histiocytic infiltrates)			
			Hepatic	2.6				
			Renal	2.6				

Table 3-1 Levels of Significant Exposure to Cadmium - Inhalation (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/m³)	LOAEL Less Serious (mg/m³)	LOAEL Serious (mg/m³)	Reference Chemical Form	Comments
22	Hamster (Golden Syrian)	30 min	Resp		1.1 (moderate increase in PMN, 2-fold increase in acid phosphatase)	10.1 (severe pneumonitis)	Henderson et al. 1979 CdCl2	
23	Rabbit (New Zealand)	2 hr	Resp		4.5 M (mild, multifocal interstitial pneumonitis)		Grose et al. 1987 CdCl2	
24	Rabbit (New Zealand)	2 hr	Resp		0.45 M (increase in alveolar macrophages)	4.5 M (multifocal interstitial pneumonitis)	Grose et al. 1987 CdO dust	
			Bd Wt		0.45 M (unspecified decrease in body weight)			
Immuno/ Lymphoret								
25	Mouse (Swiss)	2 hr		0.11 F	0.19 F (decreased humoral immune response)		Graham et al. 1978 CdCl2	
26	Mouse (C57Bl/6)	60 min			0.88 F (reduction in spleen lymphocyte viability [35%], numbers, and humoral response (75%)]		Krzystyniak et al. 1987 CdCl2	
INTERMEDIATE EXPOSURE								
Death								
27	Rat (Wistar)	20 wk 5 d/wk 5 hr/d				1 F (13/13 died by week 20)	Baranski and Sitarek 1987 CdO dusts	

Table 3-1 Levels of Significant Exposure to Cadmium - Inhalation (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/m³)	LOAEL Less Serious (mg/m³)	LOAEL Serious (mg/m³)	Reference Chemical Form	Comments
28	Rat (Fischer 344)	62 d 5 d/wk 6 hr/d				2.13 M (100% mortality by day 45)	Kutzman et al. 1986 CdCl2	
29	Rat (Wistar)	6 mo 40 hr/wk				0.09 (> 75% mortality by 11-12 months postexposure)	Oldiges et al. 1989 CdCl2	
30	Rat (Wistar)	6 mo 40 hr/wk				0.27 (> 75% mortality by 21-23 months postexposure)	Oldiges et al. 1989 CdS	
31	Rat (Wistar)	63d 24 hr/d				0.105 F (5/12 died)	Prigge 1978a CdO dust	
Systemic								
32	Rat (Wistar)	20 wk 5 d/wk 5 hr/d	Bd Wt	0.16 F		1 F (30-50% decreased body weight gain)	Baranski and Sitarek 1987 CdO dusts	
33	Rat (Wistar)	30 d 7 d/wk 22 hr/d	Resp		0.105 M (increased total bronchoalvelolar macrophage numbers, leukocytes, and macrophage cytotoxicity)		Glaser et al. 1986 CdCl2	No histopathology examination.
			Hemato		0.105 M (45% increase in WBC)			

Table 3-1 Levels of Significant Exposure to Cadmium - Inhalation (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/m³)	LOAEL Less Serious (mg/m³)	LOAEL Serious (mg/m³)	Reference Chemical Form	Comments
34	Rat (Wistar)	30 d 7 d/wk 22 hr/d	Resp		0.098 M (increased total bronchoalvelolar macrophage numbers, leukocytes, and macrophage cytotoxicity)		Glaser et al. 1986 CdO dust	No histopathology examination.
			Hemato		0.098 M (45% increase in WBC)			
35	Rat (Wistar)	30 d 7 d/wk 22 hr/d	Resp		1.034 M (increased total bronchoalvelolar macrophage numbers, leukocytes, and macrophage cytotoxicity)		Glaser et al. 1986 CdS	No histopathological examination.
			Hemato	1.034 M				
			Bd Wt	1.034 M				
36	Rat (Fischer 344)	62 d 5 d/wk 6 hr/d	Resp			1.06 M (marked fibrosis with significant increase in collagen)	Kutzman et al. 1986 CdCl2	
			Bd Wt	0.33	1.06 (14% decreased body weight)	2.13 (42-51% decreased body weight)		

Table 3-1 Levels of Significant Exposure to Cadmium - Inhalation (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/m³)	LOAEL Less Serious (mg/m³)		LOAEL Serious (mg/m³)		Reference Chemical Form	Comments
37	Rat (Fischer- 344)	6.33 hr/d 5 d/wk 13 wk	Resp		0.022 F	(epithelial degeneration in the larynx)	0.88	(marked inflammation and moderate fibrosis in interstitium around alveolar ducts and terminal bronchioles)	NTP 1995 CdO	
					0.22	(Inflammation of nasal respiratory epithelium)				
			Cardio	0.88						
			Gastro	0.88						
			Hemato	0.88						
			Hepatic	0.88						
			Renal	0.88						
			Bd Wt	0.88						
38	Rat (Fischer 344)	4 wks 5 d/wk 6 hr/d	Resp	0.1 M					Oberdorster et al. 1994 CdCl2	

Table 3-1 Levels of Significant Exposure to Cadmium - Inhalation (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/m³)	LOAEL Less Serious (mg/m³)	LOAEL Serious (mg/m³)	Reference Chemical Form	Comments
39	Rat (Wistar)	63 or 90 d 24 hr/d	Resp		0.025 F (proliferations, histiocytic cell granulomas)		Prigge 1978a CdO dust	
			Hemato		0.052 F (increased hemoglobin and hematocrit)			
			Hepatic	0.105 F				
			Renal	0.105 F				
			Bd Wt		0.105 F (11% decrease in body weight)			
			Metab		0.105 F (decreased blood pH and pO2, increased pCO2)			
40	Rat (Wistar)	21 d Gd 1-21 24 hr/d	Resp		0.204 F (77% increased lung relative weight)		Prigge 1978b CdCl2	
			Hemato		0.204 F (8% increased hemoglobin, 5% increased hematocrit)			
			Hepatic	0.581 F				
			Renal	0.581 F				
			Bd Wt	0.394 F				

Table 3-1 Levels of Significant Exposure to Cadmium - Inhalation (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/m³)	LOAEL Less Serious (mg/m³)	LOAEL Serious (mg/m³)	Reference Chemical Form	Comments
41	Rat (Wistar)	21 d Gd 1-21 24 hr/d	Resp		0.204 F (70% increased lung relative weight)		Prigge 1978b CdCl2	
			Hemato		0.581 F (increased hemoglobin [12%], hematocrit [12%], total biliurin [2-fold])			
			Hepatic	0.581 F				
			Renal	0.581 F				
			Bd Wt		0.394 F (12% decreased maternal weight gain)			
42	Mouse (B6C3F1)	6.33 hr/d 5 d/wk 13 wk	Resp		0.088 M (Degeneration of nasal olfactory epithelium)		NTP 1995 CdO	
					0.022 (alveolar histiocytic infiltrates and squamous metaplasia of the larynx)			
			Cardio	0.88				
			Gastro	0.88				
			Hepatic	0.88				
			Renal	0.88				
			Bd Wt	0.88				

Table 3-1 Levels of Significant Exposure to Cadmium - Inhalation (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/m³)	LOAEL Less Serious (mg/m³)	LOAEL Serious (mg/m³)	Reference Chemical Form	Comments
43	Mouse (BALB/c)	4 wks 5 d/wk 6 hr/d	Resp		0.1 M (increased neutrophils, LDH and beta-glucuronidase; pulmonary inflammation)		Oberdorster et al. 1994 CdCl2	
44	Rabbit (NS)	9 mo 21 d/mo 3 hr/d	Resp			4 (chronic pneumonia, emphysema)	Friberg 1950 Cd metal dust	
			Hemato		4 (eosinophilia, lower hemoglobin)			
			Renal			4 (proteinuria)		
45	Rabbit (NS)	7 mo 23 d/mo 3 hr/d	Resp			5.6 (emphysema)	Friberg 1950 Cd metal dust	
			Renal			5.6 (proteinuria in 6/10 surviving to the end of exposure)		
46	Rabbit (NS)	4-6 wk 5 d/wk 6 hr/d	Resp			0.4 M (lung interstitial inflammation, type 2 cell hyperplasia)	Johansson et al. 1984 CdCl2	

Table 3-1 Levels of Significant Exposure to Cadmium - Inhalation (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/m³)	LOAEL Less Serious (mg/m³)	LOAEL Serious (mg/m³)	Reference Chemical Form	Comments
Reproductive								
47	Rat (Wistar)	5 hr/d 5 d/wk 5 mo premating, mating, Gd 1-20		0.16 F			Baranski 1984 CdO	
48	Rat (Wistar)	20 wk 5 d/wk 5 hr/d			1 F (increased duration of estrous cycle)		Baranski and Sitarek 1987 CdO dusts	
49	Rat (Fischer 344)	62 d 5 d/wk 6 hr/d		1.06 M (t			Kutzman et al. 1986 CdCl2	
50	Rat (Fischer- 344)	6.33 hr/d 5 d/wk 13 wk		0.22 M 0.22 F	0.88 M (decreased spermatid counts 0.88 F (increased estrous cycle length)		NTP 1995 CdO	
Developmental								
51	Rat (Wistar)	5 hr/d 5 d/wk 5 mo premating, mating, Gd 1-20			0.02 F (altered performance on neurobehavioral tests)		Baranski 1984 CdO	

Table 3-1 Levels of Significant Exposure to Cadmium - Inhalation (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/m³)	LOAEL Less Serious (mg/m³)		LOAEL Serious (mg/m³)		Reference Chemical Form	Comments
52	Rat (Wistar)	4-5 mo 5 d/wk 5 hr/d			0.02	(altered performance on neurobehavioral tests)	0.16	(decreased pup viability)	Baranski 1985 CdO dusts	
53	Rat (Sprague-Dawley)	6.27 hr/d 7 d/wk Gd 4-19		0.4 F	1.7 F	(decreased fetal body weight and reduced ossification)			NTP 1995 CdO	
54	Rat (Wistar)	21 d Gd 1-21 24 hr/d			0.581	(9% decreased fetal body weight, 12% increase in fetal alkaline phosphatase)			Prigge 1978b CdCl2	
55	Mouse (Swiss)	6.27 hr/d 7 d/wk Gd 4-17		0.04 F	0.4 F	(decreased fetal body weight)			NTP 1995 CdO	
Cancer										
56	Rat (Wistar)	6 mo 40 hr/wk					0.09	(CEL: lung bronchioalveolar adenomas, adenocarcinomas, and squamous cell carcinomas)	Oldiges et al. 1989 CdCl2	
CHRONIC EXPOSURE										
Death										
57	Human	1-34 yr 5 d/wk 8 hr/d (occup)					6.8 M	(2 fatalities from 14 years or 25 years of exposure to Cd dust)	Friberg 1950 Cd dust	

Table 3-1 Levels of Significant Exposure to Cadmium - Inhalation (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/m³)	LOAEL Less Serious (mg/m³)	LOAEL Serious (mg/m³)	Reference Chemical Form	Comments
58	Rat (Wistar)	413-455 d 7 d/wk 22 hr/d				0.095 M (6/20 died)	Oldiges and Glaser 1986 CdSO4	
59	Rat (Wistar)	18 mo 7 d/wk 22 hr/d				0.03 M (>75% mortality by 12 months postexposure)	Oldiges et al. 1989 CdCl2	
60	Rat (Wistar)	18 mo 7 d/wk 22 hr/d				0.09 (more than 25% died after 7 months [M] and 11 months [F] of exposure)	Oldiges et al. 1989 CdO dust	
61	Rat (Wistar)	18 mo 7 d/wk 22 hr/d				0.09 (>75% mortality after 12 months postexposure)	Oldiges et al. 1989 CdS	
62	Rat (Wistar)	18 mo 7 d/wk 22 hr/d				0.09 M (>25% mortality by 14 months of exposure)	Oldiges et al. 1989 CdSO4	
						0.09 F (>75% by 11 months postexposure)		
Systemic								
63	Human		Renal	0.0001[c] F			Buchet et al. 1990; Jarup et al. 2000; Suwazono et al. 2006 form not specified	

Table 3-1 Levels of Significant Exposure to Cadmium - Inhalation (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/m³)	LOAEL Less Serious (mg/m³)	LOAEL Serious (mg/m³)		Reference Chemical Form	Comments
64	Human	4-24 yr 5 d/wk 8 hr/d (occup)	Resp	0.025				Edling et al. 1986 CdO fume	
65	Human	30 yr 5 d/wk 8 hr/d (occup)	Renal	0.033		0.067	(pronounced proteinuria)	Elinder et al. 1985b CdO fume	
66	Human	30 yr 5 d/wk 8 hr/d (occup)	Renal	0.0153 M		0.0379 M	(100% incidence of proteinuria in the cohort exposed to this level for 21 years)	Falck et al. 1983 CdO fume	
67	Human	30 yr 5 d/wk 8 hr/d (occup)	Renal	0.017		0.023	(9.2% incidence of proteinuria)	Jarup et al. 1988 CdO dust	
68	Human	30 yr 5 d/wk 8 hr/d (occup)	Renal	0.0367 M				Mason et al. 1988 form not specified	
69	Human	30 yr 5 d/wk 8 hr/d (occup)	Renal	0.027				Thun et al. 1989 CdO dust or fume	

Table 3-1 Levels of Significant Exposure to Cadmium - Inhalation (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/m³)	LOAEL Less Serious (mg/m³)	LOAEL Serious (mg/m³)	Reference Chemical Form	Comments
70	Rat (Wistar)	18 mo 7 d/wk 23 hr/d	Resp			0.0134 M (adenomatous hyperplasia in the bronchoalveolar area)	Takenaka et al. 1983 CdCl2	
			Bd Wt	0.0508 M				
Cancer								
71	Human	6 mo - 43 yr 7 d/wk 8 hr/d (occup)				0.1 M (CEL: 50-111 lung cancer deaths per 1000 workers; 45 year exposure)	Stayner et al. 1992 CdO dust or fumes	
72	Rat (Wistar)	18 mo 7 d/wk 22 hr/d				0.03 (CEL: lung bronchioalveolar adenomas, adenocarcinomas, and squamous cell carcinomas)	Oldiges et al. 1989 CdCl2	
73	Rat (Wistar)	18 mo 7 d/wk 22 hr/d				0.03 (CEL: lung bronchioalveolar adenomas, adenocarcinomas, and squamous cell carcinomas)	Oldiges et al. 1989 CdO dust	

Table 3-1 Levels of Significant Exposure to Cadmium - Inhalation (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/m³)	LOAEL Less Serious (mg/m³)	LOAEL Serious (mg/m³)		Reference Chemical Form	Comments
74	Rat (Wistar)	18 mo 7 d/wk 22 hr/d				0.03	(CEL: lung bronchioalveolar adenomas, adenocarcinomas)	Oldiges et al. 1989 CdO fume	
75	Rat (Wistar)	18 mo 7 d/wk 22 hr/d				0.09	(CEL: lung bronchioalveolar adenomas, adenocarcinomas, and squamous cell carcinomas)	Oldiges et al. 1989 CdS	
76	Rat (Wistar)	18 mo 7 d/wk 22 hr/d				0.09	(CEL: lung bronchio-alveolar adenomas, adenocarcinomas, squamous cell carcinomas)	Oldiges et al. 1989 CdSO4	

Table 3-1 Levels of Significant Exposure to Cadmium - Inhalation (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/m³)	LOAEL Less Serious (mg/m³)	LOAEL Serious (mg/m³)	Reference Chemical Form	Comments
77	Rat (Wistar)	18 mo 7 d/wk 23 hr/d				0.0134 M (CEL: lung epidermoid carcinomas, adenocarcinomas, and mucoepidermoid carcinomas)	Takenaka et al. 1983 CdCl2	

a The number corresponds to entries in Figure 3-1.

b Used to derive an acute-duration inhalation minimal risk level (MRL) of 0.00003 mg Cd/m3 (0.03 ug Cd/m3); concentration was adjusted for intermittent exposure (6.2 hours/day, 5 days/week) and divided by an uncertainty factor of 300 (10 for use of a LOAEL, 3 for extrapolation from animals to humans with dosimetric adjustment, and 10 for human variability).

c The chronic-duration inhalation MRL of 0.00001 mg Cd/m3 (0.01 ug Cd/m3) was calculated from the 95% lower confidence limit of the urinary cadmium level associated with a 10% increased risk of low molecular weight proteinuria (0.5 ug/g creatinine) estimated from a meta-analysis of select environmental exposure studies. An air concentration (together with an assumed dietary intake of 0.3 ug Cd/kg/day) which would result in this urinary cadmium concentration was estimated using the ICRP human respiratory tract model and a modification of the Nordberg-Kjellström pharmacokinetic model (see Appendix A for details on the meta-analysis and extrapolation to air concentration). This air concentration of 0.1 ug Cd/m3 was divided by an uncertainty factor of 3 for human variability and a modifying factor of 3.

Bd Wt = body weight; Cardio = cardiovascular; CEL = cancer effect level; d = day(s); Endocr = endocrine; F = Female; Gastro = gastrointestinal; Gd = gestational day; Hemato = hematological; hr = hour(s); Immuno/Lymphoret = immunological/lymphoreticular; LC50 = lethal concentration, 50% kill; LDH = lactate dehydrogenase; LOAEL = lowest-observed-adverse-effect level; M = male; min = minute(s); Metab = metabolic; mo = month(s); NOAEL = no-observed-adverse-effect level; NS = not specified; occup = occupational; PMN = polymorphonuclear leukocyte; Resp = respiratory; WBC = white blood cells; wk = week(s); yr = year(s)