Table 3-6 Levels of Significant Exposure to Cadmium - Oral

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
ACUTE EXPOSURE								
Death								
1	Rat (NS)	once (G)				29 (LD50 at 8 days; 2 weeks old)	Kostial et al. 1978 CdCl2	
						129 F (LD50 at 8 days; 6 weeks old)		
						104 F (LD50 at 8 days; 18 weeks old)		
2	Rat (Sprague-Dawley)	once (GW)				225 M (LD50 at 14 days)	Kotsonis and Klaassen 1977 CdCl2	
3	Rat (Sprague-Dawley)	2 wk (W)				42 M (7/9 died within 2 weeks)	Kotsonis and Klaassen 1978 CdCl2	
4	Rat (Sprague-Dawley)	once (GW)				327 M (LD50 at 24 hours; fed rats)	Shimizu and Morita 1990 CdCl2	
						107 M (LD50 at 24 hours; fasted rats)		
5	Mouse (Swiss-Webster)	once (GW)				95.5 M (LD50 at 96 hours)	Baer and Benson 1987 CdCl2	
6	Mouse (ICR)	once (GW)				112 M (5/10 died within 8 days)	Basinger et al. 1988 CdCl2	

Table 3-6 Levels of Significant Exposure to Cadmium - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
Systemic								
7	Rat (Wistar)	10 d Gd 7-16 once (GW)	Bd Wt	2 F	12 F (14% decreased maternal body weight)		Baranski 1985 CdCl2	
8	Rat (Sprague-Dawley)	10 d 1 x/d (GW)	Hemato	31.3 M 138 F	65.6 M (increased hemoglobin, hematocrit, erythrocytes)		Borzelleca et al. 1989 CdCl2	
			Hepatic	65.6 M		138 M (focal necrosis of hepatocytes)		
			Renal			15.3 (focal necrosis of tubular epithelium)		
			Bd Wt		15.3 M (18% decreased body weight)	31.3 M (23% decreased body weight)		
				31.3 F	65.6 F (18% decreased body weight)			
9	Rat (Sprague-Dawley)	10 d (W)	Hepatic	13.9			Borzelleca et al. 1989 CdCl2	
			Renal	13.9				
			Bd Wt	13.9				
				1.1 M	7.8 M (14% decreased body weight)	11.2 M (25% decreased body weight)		

Table 3-6 Levels of Significant Exposure to Cadmium - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
10	Rat (Sprague-Dawley)	once (GW)	Cardio	150 M			Kotsonis and Klaassen 1977 CdCl2	
			Hemato	150 M				
			Hepatic	150 M				
			Renal		25 M (50% decrease in urine flow for first 2 days)			
			Bd Wt	100	150 M (initial 12% decreased body weight)			
11	Rat (Long- Evans)	Gd 6-15 (GW)	Gastro	6.13 F		61.32 F (intestinal necrosis, hemorrhage, ulcers)	Machemer and Lorke 1981 CdCl2	
			Bd Wt	1.84 F	6.13 F (27% decrease in body weight gain during treatment)	18.39 F (persistent 50% decrease in maternal body weight gain)		
12	Rat (Long- Evans)	Gd 6-15 (F)	Gastro	12.5 F			Machemer and Lorke 1981 CdCl2	
			Bd Wt	3.5 F	12.5 F (transient 19% decrease in maternal body weight gain during treatment)			
13	Rat (Wistar)	12 d (W)	Hemato		12 M (anemia)		Sakata et al. 1988 CdCl2	

Table 3-6 Levels of Significant Exposure to Cadmium - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
14	Rat (Sprague-Dawley)	once (GW)	Hepatic		75 M (focal degeneration and necrosis of parenchymal cells)		Shimizu and Morita 1990 CdCl2	
15	Mouse (CBA/Bom)	once (GW)	Gastro	15.7 M	30.4 M (gastritis and enteritis)	88.8 M (severe gastric necrosis)	Andersen et al. 1988 CdCl2	
			Hepatic	15.7 M	30.4 M (fatty infiltration of liver cells, occasional hepatocellular necrosis)			
			Renal	59.6		88.8 M (tubular necrosis and casts)		
16	Mouse (ICR)	once (GW)	Gastro			112 M (glandular stomach epithelial necrosis)	Basinger et al. 1988 CdCl2	
			Hepatic			112 M (extensive hepatocellular coagulative necrosis)		
			Renal	112 M				
Immuno/ Lymphoret								
17	Rat (Sprague-Dawley)	10 d 1 x/d (GW)		65.6 M 31.3 F	65.6 F (increased leukocyte counts)		Borzelleca et al. 1989 CdCl2	
Neurological								
18	Rat (Sprague-Dawley)	once (GW)		25 M	50 M (decreased motor activity)		Kotsonis and Klaassen 1977 CdCl2	

Table 3-6 Levels of Significant Exposure to Cadmium - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
Reproductive								
19	Rat (Wistar)	once (GW)		50 M		100 M (testicular necrosis)	Bomhard et al. 1987 CdCl2	
20	Rat (Sprague-Dawley)	10 d 1 x/d (GW)		138 F		65.6 M (testicular atrophy and loss of spermatogenic elements)	Borzelleca et al. 1989 CdCl2	
21	Rat (Sprague-Dawley)	once (GW)		25 M			Dixon et al. 1976 CdCl2	
22	Rat (Sprague-Dawley)	once (GW)		50 M		100 M (testicular necrosis; decreased spermatogenesis; decreased number females producing pups)	Kotsonis and Klaassen 1977 CdCl2	
23	Mouse (CBM/ Bom)	once (GW)		30.3 M		59.6 M (testicular necrosis)	Andersen et al. 1988 CdCl2	
Developmental								
24	Rat (Wistar)	10 d Gd 7-16 once (GW)			2 F (delayed ossification of the sternum and ribs)	40 (fused lower limbs, absent limbs, decreased number of live fetuses, increased number of resorptions)	Baranski 1985 CdCl2	

Table 3-6 Levels of Significant Exposure to Cadmium - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)		Reference Chemical Form	Comments
25	Rat (Long- Evans)	1 x/d Gd 6-15 (GW)		6.13		18.39	(increased number of fetuses with malformations)	Machemer and Lorke 1981 CdCl2	
26	Rat (Long- Evans)	10 d Gd 6-15 (F)		12.5				Machemer and Lorke 1981 CdCl2	
INTERMEDIATE EXPOSURE									
Death									
27	Rat (Wistar)	14 wk 5 d/wk (GW)				40 F	(4/13 died by week 8; 7/13 by week 14)	Baranski and Sitarek 1987 CdCl2	
28	Mouse (Swiss)	280 d (W)				1.9 F	(24/41 died by 280 days)	Blakley 1986 CdCl2	
Systemic									
29	Monkey (Rhesus)	10 wk (F)	Bd Wt	5 M				Chopra et al. 1984 CdCl2	
30	Rat (Wistar)	14 wk 5 d/wk (GW)	Bd Wt	4 F		40 F	(29% decreased maternal body weight)	Baranski and Sitarek 1987 CdCl2	
31	Rat (Sprague-Dawley)	2-10 mo (W)	Renal			30 F	(B2-microglobulinuria)	Bernard et al. 1988a CdCl2	

Table 3-6 Levels of Significant Exposure to Cadmium - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
32	Rat (Wistar)	daily 12 mo (W)	Musc/skel	0.2 M	0.5 M (increased lumbar spine deformities, decreased in lumbar spine and femur mineralization, altered bone turnover parameters)		Brzoska and Moniuszko-Jakoniuk 2005a, 2005b; Brzoska et al. 2010 CdCl2	
33	Rat (Wistar)	daily 12 mo (W)	Musc/skel		0.2 F[b] (decreased bone mineralization, mechanical properties of tibia and femur, and altered bone turnover parameters)		Brzoska and Moniuszko-Jakoniuk 2005d; Brzoska et al. 2005a, 2005c CdCl2	
34	Rat (Wistar)	daily 12 mo (W)	Musc/skel		0.3 F (alterations in bone mineral content and density and mechanical properties of lumbar vertebral and femoral bones)		Brzoska et al. 2004b, 2005b CdCl2	
35	Rat (Sprague-Dawley)	4 or 7 mo (W)	Renal			15.2 F (albuminuria, transferrinuria, B2-microglobulinuria)	Cardenas et al. 1992a CdCl2	
36	Rat (Sprague-Dawley)	190 d (W)	Cardio		1.4 M (20% increase in diastolic blood pressure)		Carmignanti and Boscolo 1984 Cd acetate	
			Bd Wt	2.8 M				

Table 3-6 Levels of Significant Exposure to Cadmium - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
37	Rat (Sprague-Dawley)	12 wk (W)	Hepatic		8.58 M (necrosis of central lobules)		Cha 1987 CdCl2	
			Renal		8.58 M (necrosis of proximal tubular epithelial cells and cloudy swelling)			
			Bd Wt		8.58 M (23% decreased in body weight gain; 9% total body weight decrease)			
38	Rat (Wistar)	170 d (W)	Bd Wt	56 F			Cifone et al. 1989a CdCl2	
39	Rat (Sprague-Dawley)	3 mo (W)	Hemato		2 (anemia)		Decker et al. 1958 CdCl2	
			Bd Wt		2 F (15% decreased body weight)	2 M (25% decreased body weight)		
40	Rat (Wistar)	4-60 wk (W)	Renal		1.18 (vesiculation of proximal tubules)		Gatta et al. 1989 CdCl2	
41	Rat	4 wk (F)	Hemato		2.5 M (anemia)		Groten et al. 1990 CdCl2	
			Renal	2.5 M				

Table 3-6 Levels of Significant Exposure to Cadmium - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
42	Rat (Wistar)	120 d (W)	Hemato		3.6 M (anemia)		Itokawa et al. 1974 CdCl2	
			Renal		3.6 M (tubular necrosis and casts, glomerular adhesions)			
43	Rat (Sprague-Dawley)	7 wk (F)	Cardio			2.5 M (congested myocardium, separation of muscle fibers)	Jamall et al. 1989 CdCl2	
			Renal	2.5 M				
			Bd Wt	2.5 M				
44	Rat (Wistar)	90 d (W)	Hemato		8 F (anemia)		Kawamura et al. 1978 CdCl2	
			Musc/skel		8 F (osteomalacia changes)			
			Renal		8 F (decreased renal clearance)			
			Endocr	8 F				
			Bd Wt		8 F (12% decreased body weight)			
45	Rat (Sprague-Dawley)	22 d Gd 0-21 (W)	Hemato		1.5 F (slight anemia)		Kelman et al. 1978 form not specified	
			Musc/skel	3.8 F				

Table 3-6 Levels of Significant Exposure to Cadmium - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
46	Rat (Sprague-Dawley)	24 wk (W)	Resp	8 M			Kotsonis and Klaassen 1978 CdCl2	
			Cardio	8 M				
			Gastro	8 M				
			Hemato	8 M				
			Musc/skel	8 M				
			Hepatic	8 M				
			Renal	1.2 M		3.1 M (proteinuria, slight focal tubular necrosis)		
			Endocr	8 M				
			Bd Wt	8 M				
47	Rat (Wistar)	8 weeks daily (W)	Hepatic		18 M (increased serum and liver triglyceride levels; increased serum cholesterol levels)		Larregle et al. 2008 CdCl2	
48	Rat (Wistar)	3 mo (F)	Cardio	3			Loeser and Lorke 1977a CdCl2	
			Hemato	3				
			Hepatic	3				
			Renal	3				
			Endocr	3				
			Bd Wt	3				

Table 3-6 Levels of Significant Exposure to Cadmium - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
49	Rat (Sprague-Dawley)	6-16 wk (W)	Resp			2.4 (lung fibrosis)	Miller et al. 1974b CdCl2	
50	Rat (Sprague-Dawley)	6 wk 5 d/wk 1 x/d (GW)	Hepatic	0.25 M			Muller et al. 1988 Cd acetate	
			Bd Wt	0.25 M				
51	Rat (NS)	4 wk (W)	Hemato		0.8 F (decreased hematocrit and hemoglobin)		Ogoshi et al. 1989 CdCl2	
			Musc/skel		0.8 F (decreased bone strength in young animals)			
			Bd Wt	0.8	1.6 F (10% decreased body weight gain)			
52	Rat (NS)	200 d (W)	Resp	0.6 M	1.2 M (reduced static compliance, lung lesions)		Petering et al. 1979 CdCl2	
53	Rat (Sprague-Dawley)	120 d (W)	Resp			3.62 M (emphysema)	Petering et al. 1979 CdCl2	

Table 3-6 Levels of Significant Exposure to Cadmium - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
54	Rat (Sprague-Dawley)	111 d (90 d prior to Gd 1-21) (W)	Hemato	5.23 F			Petering et al. 1979 CdCl2	
55	Rat (Sprague-Dawley)	Gd 1- Ld 1 (F)	Bd Wt			19.7 F (77-80% decreased maternal weight gain)	Pond and Walker 1975 CdCl2	
56	Rat (Wistar)	90 d (W)	Resp	16 F			Prigge 1978a CdCl2	
			Hemato		4 F (23% decreased serum iron)			
			Renal	4 F	8 F (35% increase in urine protein)			
			Bd Wt	8 F				
57	Rat (Wistar)	12, 26, 50, or 100 d (W)	Hemato			12 M (iron deficient anemia)	Sakata et al. 1988 CdCl2	
58	Rat (Sprague-Dawley)	7-12 mo (W)	Renal	13 F			Viau et al. 1984 CdCl2	
			Bd Wt	13 F				

Table 3-6 Levels of Significant Exposure to Cadmium - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
59	Mouse (CF1)	252 d (F)	Musc/skel		0.65 F (decrease in femur calcium content in mice undergoing repeated pregnancy/lactation periods)		Bhattacharyya et al. 1988a, 1988b	
60	Mouse (C57BL/6)	3-11 wk (W)	Bd Wt			12.5 M (63% decreased body weight gain)	Malave and de Ruffino 1984 CdCl2	
61	Mouse (B6C3F1)	16-46 wk (W)	Bd Wt			232 M (45% decreased body weight)	Waalkes et al. 1993 CdCl2	
62	Mouse (QS/CH)	Gd 1-19 (W)	Hemato	4.8 F	9.6 F (anemia)		Webster 1978 CdCl2	
			Bd Wt	4.8 F	9.6 F (14% decrease in maternal weight gain)			
63	Dog (Beagle)	3 mo (F)	Cardio	0.75			Loeser and Lorke 1977b CdCl2	
			Hemato	0.75				
			Hepatic	0.75				
			Renal	0.75				
			Bd Wt	0.75				

Table 3-6 Levels of Significant Exposure to Cadmium - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
64	Rabbit (New Zealand)	9 mo (W)	Cardio		1.6 M (increased aortic resistance, reduced contractility)		Boscolo and Carmignani 1986 CdCl2	
			Renal	1.6 M				
			Bd Wt	1.6 M				
65	Rabbit (New Zealand and Belgian Giant)	200 d (W)	Hemato		14.9 M (anemia)		Stowe et al. 1972 CdCl2	
			Hepatic		14.9 M (focal hepatic fibrosis and biliary hyperplasia)			
			Renal			14.9 M (tubular necrosis, glomerular and interstitial fibrosis)		
			Endocr	14.9				
			Bd Wt		14.9 M (11% decrease in body weight)			
Immuno/ Lymphoret								
66	Monkey (Rhesus)	10 wk (F)			5 M (increased cell-mediated immune response)		Chopra et al. 1984 CdCl2	
67	Rat (Wistar)	170 d (W)			28 F (biphasic decrease then increase in natural killer cell activity)		Cifone et al. 1989a CdCl2	

Table 3-6 Levels of Significant Exposure to Cadmium - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
68	Rat (Wistar)	3 mo (F)		3			Loeser and Lorke 1977a CdCl2	
69	Mouse (BDF1)	3 wk (W)		1.4 F	2.8 F (decreased humoral immune response)		Blakley 1985 CdCl2	
70	Mouse (Swiss)	280 d (W)			1.9 F (greater susceptibility to murine lymphocytic leukemia virus)		Blakley 1986 CdCl2	
71	Mouse (BDF1)	26 d (W)		12.5 F			Blakley 1988 CdCl2	
72	Mouse (Swiss-Webster)	30 d (W)		22 M			Bouley et al. 1984 Cd acetate	
73	Mouse (Swiss-Webster)	10 wk (W)		57 M			Exon et al. 1986 CdCl2, Cd acetate, or Cd sulfate	
74	Mouse (C57BL/6N)	12-16 wk (W)		19 F	57 F (reduced number of SRBC-activated, plaque-forming cells)		Krzystyniak et al. 1987 CdCl2	

Table 3-6 Levels of Significant Exposure to Cadmium - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
75	Mouse (C57BL/6)	3-11 wk (W)			12.5 M (decreased suppressor cell activity)		Malave and de Ruffino 1984 CdCl2	
76	Mouse (ICR)	10 wk (W)			0.75 M (induction of anti-nuclear autoantibodies)		Ohsawa et al. 1988 CdCl2	
Neurological								
77	Rat (Wistar)	14 wk 5 d/wk (GW)		4 F	40 F (aggressive behavior)		Baranski and Sitarek 1987 CdCl2	
78	Rat (Sprague-Dawley)	3-24 wk (W)		1.2 M	3.1 M (decreased motor activity)		Kotsonis and Klaassen 1978 CdCl2	
79	Rat (Sprague-Dawley)	55 d (F)		1 M	5 M (increased passive avoidance)		Nation et al. 1984 CdCl2	
80	Rat (Sprague-Dawley)	60 d (F)			9 M (decreased motor activity)		Nation et al. 1990 CdCl2	
Reproductive								
81	Rat (Wistar)	14 wk 5 d/wk (GW)		4 F	40 F (increased duration of estrus cycle)		Baranski and Sitarek 1987 CdCl2	

Table 3-6 Levels of Significant Exposure to Cadmium - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
82	Rat (Wistar)	11 wk 5 d/wk (GW)		4 F			Baranski et al. 1983 CdCl2	
83	Rat (Wistar)	10 wk 1 x/wk (GW)		5 M			Bomhard et al. 1987 CdCl2	Histopathology only.
84	Rat (Sprague-Dawley)	12 wk (W)			8.58 M (necrosis and atrophy of seminiferous tubule epithelium)		Cha 1987 CdCl2	
85	Rat	4 wk (F)		2.5 M			Groten et al. 1990 CdCl2	Histopathology only.
86	Rat (albino)	4 wk (W)		4.8 F			Kostial et al. 1993 CdCl2	
87	Rat (Sprague-Dawley)	24 wk (W)		8 M			Kotsonis and Klaassen 1978 CdCl2	
88	Rat (Wistar)	3 mo (F)		3			Loeser and Lorke 1977a CdCl2	Histopathology only.
89	Rat (NS)	120 d (W)			12.6 M (decreased sperm count and motility, seminiferous tubular damage)		Saxena et al. 1989 Cd acetate	

Table 3-6 Levels of Significant Exposure to Cadmium - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
90	Rat (Long- Evans)	70-80 d (W)		4.64 M			Zenick et al. 1982 CdCl2	
91	Dog (Beagle)	3 mo (F)		0.75			Loeser and Lorke 1977b CdCl2	
Developmental								
92	Rat (Wistar)	21 d Gd 1-21 (W)			0.706 (delayed development of sensory motor coordination reflexes; increased motor activity)		Ali et al. 1986 Cd acetate	
93	Rat (Wistar)	20 d Gd 1-20 (W)			9.6 (decreased fetal body weight [12%], body length [7%], and hematocrit [13%])		Baranski 1987 CdCl2	Decreased maternal water and food consumption.
94	Rat (Wistar)	11 wk 5 d/wk 1 x/d (GW)			0.04 (pup behavioral alterations)		Baranski et al. 1983 CdCl2	

Table 3-6 Levels of Significant Exposure to Cadmium - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg)	LOAEL Less Serious (mg/kg)	LOAEL Serious (mg/kg)	Reference Chemical Form	Comments
95	Rat (Wistar)	11-94 d Gd 5-15 Ld 2-28 1 x/d ppd 1-56 5 d/wk 1 x/d (GW)			14 M (decreased horizontal ambulation and rearing activity; increased frequency of somatosensory, visual, and auditory electrocorticogram; prolonged latency and duration of evoked potentials)		Desi et al. 1998 CdCl2	
96	Rat (Druckery)	Gd 0- Ld 21 (W)			5 (decreased pup brain and body weight at 7, 14, and 21 days)		Gupta et al 1993 Cd acetate	
97	Rat (Sprague-Dawley)	Gd 0-20 (W)			1.5 (12% decreased hematocrit)		Kelman et al. 1978 form not specified	
98	Rat (albino)	10 wk (W)			4.8 (12% decrease in pup body weight at weaning)		Kostial et al. 1993 CdCl2	
99	Rat (Wistar)	approx. 49 d 4 wk old through mating 7 d/wk 1 x/d (GO)			7 M (alterations in ambulation behavior; prolonged latency and duration of somatosensory evoked potentials)		Nagymajtenyi et al. 1997 CdCl2	

Table 3-6 Levels of Significant Exposure to Cadmium - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
100	Rat (Sprague-Dawley)	60 d prior to Gd 1 or Gd 1-21 (W)			2.61 (decreased live birth weight)		Petering et al. 1979 CdCl2	
101	Rat (Sprague-Dawley)	Gd 1- Ld 1 (F)			19.7 (13-19% decreased pup birth weight)		Pond and Walker 1975 CdCl2	
102	Rat (ITRC)	21 d Gd 0-20 (W)		21			Saxena et al. 1986 Cd acetate	
103	Rat (Sprague-Dawley)	15 d Gd 6-20 (W)		0.63	4.7 (8% decreased fetal body weight)		Sorell and Graziano 1990 CdCl2	
104	Rat (Sprague-Dawley)	9 wk 1 x/d (GW)		1	10 (delayed ossification, decreased body weight)		Sutou et al. 1980 form not specified	
105	Mouse (QS/CH)	19 d Gd 1-19 (W)			2.4 (decreased fetal body weight; severe anemia)		Webster 1978 CdCl2	
CHRONIC EXPOSURE								
Systemic								
106	Human		Renal	0.0003[c] F			Buchet et al. 1990; Jarup et al. 2000; Suwazono et al. 2006 form not specified	

Table 3-6 Levels of Significant Exposure to Cadmium - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
107	Human	NS lifetime (F)	Renal	0.0021			Nogawa et al. 1989 form not specified	
108	Human	>25 yr lifetime (environ)	Hemato	0.0078			Shiwen et al. 1990 Cd metal	
			Musc/skel	0.0078				
			Renal		0.0078 (increased excretion of low molecular weight proteins)			
109	Monkey (Rhesus)	9 yr (F)	Cardio	0.53 M	1.71 M (increased blood pressure during the first 1.5 years)		Akahori et al. 1994 CdCl2	
110	Rat (Sprague-Dawley)	18 mo (W)	Renal			13 F (loss of glomerular polyanion charge barrier, proteinuria)	Bernard et al. 1992 CdCl2	
111	Rat (Wistar)	72 wk (F)	Renal	3.5	17.5 (8 to 9-fold increase in LDH and GST starting at 13 weeks)		Bomhard et al. 1984 CdCl2	

Table 3-6 Levels of Significant Exposure to Cadmium - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
112	Rat (Wistar)	daily 24 mo (W)	Musc/skel		0.08 F (decreases in bone mineral content and density of lumbar spine, altered bone turnover paramters, increases in deformed and fractured vertebral bodies)		Brzoska and Moniuszko-Jakoniuk 2004a, 2004b; Brzoska 2011 CdCl2	
113	Rat (Sprague-Dawley)	12 mo (W)	Hemato	0.79			Decker et al. 1958 CdCl2	
			Bd Wt	0.79				
114	Rat (Sprague-Dawley)	M: 92 wk F: 84 wk (W)	Cardio	4.01			Fingerle et al. 1982 CdCl2	
			Renal	0.8	1.51 (proximal tubule lesions)			
			Bd Wt	4.01				
115	Rat (Sprague-Dawley)	6, 12, or 18 mo (W)	Cardio	2.281 F			Mangler et al 1988 CdCl2	
			Hepatic	2.281 F				
			Renal		2.337 F (cloudy swelling of tubular cells)			
			Bd Wt	2.281 F				

Table 3-6 Levels of Significant Exposure to Cadmium - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
116	Rat (Wistar)	31 mo (W)	Musc/skel			3.6 (muscle atrophy)	Sato et al. 1978 CdCl2	
			Bd Wt	3.6				
117	Rat (Wistar)	2 yr (W)	Renal	2.6 M			Shaikh et al. 1989 CdCl2	
118	Rat (Wistar)	77 wk (F)	Bd Wt	3.5 M	7 M (10% decreased body weight)		Waalkes and Rehm 1992 CdCl2	
119	Mouse (CF1)	18 months (F)	Musc/skel	0.65 F	6.5 F (loss of bone calcium in ovariectomized mice)		Bhattacharyya et al. 1988c	
120	Mouse (CBA/H)	12 mo (W)	Hemato			57 (anemia and bone marrow hypoplasia)	Hays and Margaretten 1985 form not specified	
			Renal	57				
			Bd Wt			57 (21% decreased terminal body weight)		
Neurological								
121	Rat (Wistar)	31 mo (W)				3.6 (peripheral neuropathy)	Sato et al. 1978 CdCl2	

Table 3-6 Levels of Significant Exposure to Cadmium - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
Cancer								
122	Rat (Wistar)	77 wk (F)				3.5 M (CEL: increased rates of prostatic adenomas)	Waalkes and Rehm 1992 CdCl2	

a The number corresponds to entries in Figure 3-2.

b The intermediate-duration oral MRL of 0.0005 mg Cd/kg/day (0.5 ug Cd/kg/day) was calculated using a benchmark dose analysis. The BMDL1std of 0.05 mg Cd/kg/day was divided by an uncertainty factor of 100 (10 to account for extrapolation from animals to humans and 10 for human variability).

c The chronic-duration oral MRL of 0.0001 mg Cd/kg/day (0.1 ug Cd/kg/day) 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 intake which would result in this urinary cadmium concentration was estimated using a modification of the Nordberg-Kjellström pharmacokinetic model (see Appendix A for details on the meta-analysis and extrapolation to dietary intake). This dose of 0.3 ug/kg/day was divided by an uncertainty factor of 3 for human variability.

Bd Wt = body weight; Cardio = cardiovascular; CEL = cancer effect level; d = day(s); Endocr = endocrine; (F) = feed; F = Female; (G) = gavage; Gastro = gastrointestinal; Gd = gestational day; (GO) = gavage in oil; GST = glutathione-S-transferase; (GW) = gavage in water; Hemato = hematological; Immuno/Lymphoret = immunological/lymphoreticular; LD50 = lethal dose, 50% kill; LDH = Lactate dehydrogenase; LOAEL = lowest-observed-adverse-effect level; M = male; mo = month(s); Musc/skel = musculoskeletal; NOAEL = no-observed-adverse-effect level; NS = not specified; ppd = post-parturition day; Resp = respiratory; SRBC = sheep red blood cells; (W) = drinking water; wk = week(s); x = time(s); yr = year(s)