

Table 3-2 Levels of Significant Exposure to Uranium - Oral

Key to Figure	Species ^a (Strain)	Exposure/Duration/Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL		Reference Chemical Form	Comments
					Less Serious (mg/kg/day)	Serious (mg/kg/day)		
ACUTE EXPOSURE								
Death								
1	Rat (Sprague-Dawley)	once (GW)				114 M (LD50)	Domingo et al. 1987 Uranyl Acetate	
2	Rat (NS)	once (F)				664 (16% mortality)	Maynard et al. 1953 Uranyl Nitrate	
3	Mouse (Swiss-Webster)	once (GW)				136 M (LD50)	Domingo et al. 1987 Uranyl Acetate	
4	Mouse (BALB/c)	once (G)				166 M (100% mortality 3 days post exposure)	Martinez et al. 2003 Uranyl Nitrate	
Systemic								
5	Human	once (W)	Gastro		14.3 M (nausea, vomiting, diarrhea)		Butterworth 1955 Uranyl Nitrate	
6	Rat (Long-Evans)	2 wk ad lib (W)	Bd Wt	14 M		28 M (53% reduced body weight gain)	Briner and Murray 2005 Depleted uranyl acetate	

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					Less Serious (mg/kg/day)	Serious (mg/kg/day)		
7	Rat (Sprague-Dawley)	once (GW)	Hepatic		118 M (microhemorrhagic foci)		Domingo et al. 1987 Uranyl Acetate	
			Renal		118 M (Increased urine volume, increased plasma creatinine and urea, increased urinary total protein and creatinine, and minimal histological lesions)			
			Bd Wt		118 M (weight loss)			
8	Rat (Sprague-Dawley)	1 or 3 d (GW)	Metab		97 M (alterations in serum 1,25(OH) ₂ vitamin D levels)		Tissandie et al. 2006 Uranyl Nitrate	
9	Mouse (BALB/c)	once (G)	Renal		166 M (increased blood urea and creatinine levels, tubular necrosis)		Martinez et al. 2003 Uranyl Nitrate	
10	Mouse (Swiss)	5 d (F)	Renal		508 M (increased blood urea nitrogen, creatinine, and alkaline phosphatase levels)		Ozmen and Yurekli 1998 Uranyl Nitrate	
			Bd Wt	508 M				

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					Less Serious (mg/kg/day)	Serious (mg/kg/day)		
Neurological								
11	Rat (Long-Evans)	2 wk ad lib (W)		14 M	28 M (increased open field activity)		Briner and Murray 2005 Depleted uranyl acetate	
12	Mouse (Swiss-Webster)	2 wk ad lib (W)			6 F (increased open field activity)		Briner 2009 Depleted uranyl acetate	
Developmental								
13	Rat (Wistar)	once (GW)			42.7 (delayed tooth eruption and development in neonatal rats)		Pujadas-Bigi et al. 2003 Uranyl Nitrate	
14	Mouse (Swiss-Webster)	Gd 6-15 (GW)			2.8 ^b (decreased fetal BW; increased incidence of external defects)		Domingo et al. 1989c Uranyl Acetate	
INTERMEDIATE EXPOSURE								
Death								
15	Rat (NS)	30 d (F)				827 M (LD50)	Maynard and Hodge 1949 Uranium Peroxide	
16	Rat (NS)	30 d (F)				658 M (LD50) 1096 F (LD50)	Maynard and Hodge 1949 Uranium Tetrachloride	
17	Rat (NS)	30 d (F)				541 (LD50)	Maynard and Hodge 1949 Uranyl Fluoride	

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					Less Serious (mg/kg/day)	Serious (mg/kg/day)		
18	Rat (NS)	30 d (F)				7858 M (100% mortality) 1103 F (LD50)	Maynard and Hodge 1949 Uranyl Acetate	
19	Rat (NS)	30 d (F)				1579 (LD50)	Maynard and Hodge 1949 Uranyl Nitrate	
20	Rat (NS)	30 d (F)				664 (increased mortality)	Maynard et al. 1953 Uranyl Nitrate	
21	Mouse (Swiss- Webster)	30 d 1x/d (G)				2.8 F (10% mortality)	Domingo et al. 1989b Uranyl Acetate	
22	Mouse (dba)	48 wk ad lib (F)				452 F (8% mortality)	Tannenbaum et al. 1951 Uranyl Fluoride	
23	Mouse (dba)	48 wk ad lib (F)				925 F (24% mortality)	Tannenbaum et al. 1951 Uranyl Nitrate	
24	Dog (Beagle)	30 d 6 d/wk (F)				440 (lethal dose)	Maynard and Hodge 1949 Uranium Dioxide	
25	Dog (Beagle)	30 d 6 d/wk (F)				390 (lethal dose)	Maynard and Hodge 1949 Uranium Peroxide	

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					Less Serious (mg/kg/day)	Serious (mg/kg/day)		
26	Dog (Beagle)	30 d 6 d/wk (F)				5653	(lethal dose)	Maynard and Hodge 1949 Triuranium Octoxide
27	Dog (Beagle)	30 d 6 d/wk (F)				63	(lethal dose)	Maynard and Hodge 1949 Uranium Tetrachloride
28	Dog (Beagle)	30 d 6 d/wk (F)				15.4	(lethal dose)	Maynard and Hodge 1949 Uranyl Fluoride
29	Dog (Beagle)	30 d 6 d/wk (F)				237	(lethal dose)	Maynard and Hodge 1949 Uranyl Nitrate
30	Dog (NS)	138 d (F)				95	(lethal dose)	Maynard and Hodge 1949 Uranyl Nitrate
31	Dog (Beagle)	30 d 6 d/wk (F)				191	(lethal dose)	Maynard and Hodge 1949 Ammonium Diuranate
32	Dog (Beagle)	30 d 6 d/wk (F)				190	(lethal dose)	Maynard and Hodge 1949 Sodium Uranate
33	Rabbit (NS)	30 d (F)				14.2	(67% mortality)	Maynard and Hodge 1949 Uranyl Nitrate

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					Less Serious (mg/kg/day)	Serious (mg/kg/day)		
Systemic								
34	Rat (Sprague-Dawley)	1.5 mo ad lib (W)	Bd Wt	2 M			Bensoussan et al. 2009 Uranyl Nitrate	
35	Rat (Sprague-Dawley)	9 mo (W)	Hemato		2.4 M (20% decreased in erythrocyte levels)		Berradi et al. 2008 Depleted uranyl nitrate	
			Renal		2.4 M (tubulointerstitial lesions)			
36	Rat (Long-Evans)	6 mo ad lib (W)	Bd Wt	14 M		28 M (46% reduced body weight gain)	Briner and Murray 2005 Depleted uranyl acetate	
37	Rat (Sprague-Dawley)	9 mo ad lib (W)	Bd Wt		2.7 M (11% reduced final body weight)		Bussy et al. 2006 Depleted uranyl nitrate	

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					Less Serious (mg/kg/day)	Serious (mg/kg/day)		
38	Rat (Sprague- Dawley)	28 d (W)	Resp	35.3 M			Gilman et al. 1998a Uranyl Nitrate	
			Cardio	35.3 M				
			Gastro	35.3 M				
			Hemato	35.3 M				
			Musc/skel	35.3 M				
			Hepatic	35.3 M				
			Renal	35.3 M	40 F (39% increase in serum uric acid)			
			Endocr	35.3 M				
Bd Wt	35.3 M							

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					Less Serious (mg/kg/day)	Serious (mg/kg/day)		
39	Rat (Sprague- Dawley)	91 d (W)	Resp	36.73 M			Gilman et al. 1998a Uranyl Nitrate	
			Cardio	36.73 M				
			Gastro	36.73 M				
			Hemato	36.73 M				
			Musc/skel	36.73 M				
			Hepatic		0.06 M (anisokaryosis, vesiculation, increased portal density, perivenous vacuolation and homogeneity)			
			Renal		0.06 ^c M (nuclear vesiculation, cytoplasmic vacuolation, tubular dilation, interstitial lymphoid cuffing)			
			Endocr	0.06 M 0.42 F	0.31 M (multifocal reduction of follicular size, increased epithelial height in thyroid, decreased amount and density of colloid)			
					2.01 F (multifocal reduction of follicular size, increased epithelial height in thyroid, decreased amount)			
			Bd Wt	36.73 M				
Other	7.54 M	36.73 M (sinus hyperplasia in spleen)						

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					Less Serious (mg/kg/day)	Serious (mg/kg/day)		
40	Rat (Sprague- Dawley)	3 months ad lib (W)	Bd Wt	22.5 M			Linares et al. 2005 Uranyl Acetate	
41	Rat (NS)	30 d (F)	Bd Wt			6637 (retarded growth)	Maynard et al. 1953 Uranyl Nitrate	
42	Rat (Sprague- Dawley)	4 wk (W)	Hemato	4.5 M	9 M (5.3 % increased hematocrit, 9% increased mean corpuscular hemoglobin concentration, 7% increased erythrocytes)		Ortega et al. 1989a Uranyl Acetate	
			Hepatic	2.2 M	4.5 M (28% increased blood glucose; 34% increased SGOT, 32% increased SGPT)			
			Renal		1.1 M (6% increased total plasma proteins)			
43	Rat (Sprague- Dawley)	9 mo (W)	Hepatic	1 M			Racine et al. 2010 Depleted uranyl nitrate	
			Metab		1 M (altered cholesterol catabolism)			

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					Less Serious (mg/kg/day)	Serious (mg/kg/day)		
44	Rat (Sprague-Dawley)	90 months (W)	Renal	2.3 M			Rouas et al. 2011 Depleted uranyl nitrate	
45	Rat (Sprague-Dawley)	9 mo (W)	Metab		2.4 M (decreased 1,25(OH)vitamin D3 levels)		Tissandie et al. 2007 Depleted uranyl nitrate	
46	Mouse (C57BL/6N)	15 wk ad lib (W)	Bd Wt	100 F			Arnault et al. 2008 Uranyl Nitrate	
47	Mouse (B6C3F1)	30 d ad lib (W)	Bd Wt	9.3 F			Raymond-Whish et al. 2007 Depleted uranyl nitrate	
48	Mouse (dba)	48 wk ad lib (F)	Renal		452 M (nodular development on kidney surface)		Tannenbaum et al. 1951 Uranyl Fluoride	
49	Mouse (C3H)	18 wk ad lib (F)	Bd Wt	925 F			Tannenbaum et al. 1951 Uranyl Nitrate	
			Other	925 F				
50	Mouse (C3H)	48 wk ad lib (F)	Renal		452 M (nodular development on kidney surface)		Tannenbaum et al. 1951 Uranyl Fluoride	

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					Less Serious (mg/kg/day)	Serious (mg/kg/day)		
51	Mouse (dba)	48 wk ad lib (F)	Bd Wt	462 F			Tannenbaum et al. 1951 Uranyl Nitrate	
			Other	462 F				
52	Rabbit (New Zealand)	91 d (W)	Resp	28.7 M			Gilman et al. 1998b Uranyl Nitrate	
			Cardio	28.7 M				
			Gastro	28.7 M				
			Hemato	28.7 M				
			Musc/skel	28.7 M				
			Hepatic	28.7 M				
			Renal		0.05 M (cytoplasmic vacuolization, anisokaryosis, nuclear vesiculation)			
					0.49 F (anisokaryosis, nuclear vesiculation, atrophy)			
Endocr	28.7 M							
Bd Wt	28.7 M							

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					Less Serious (mg/kg/day)	Serious (mg/kg/day)			
53	Rabbit (New Zealand)	91 d (W)	Resp	40.98 M			Gilman et al. 1998c Uranyl Nitrate		
			Cardio	40.98 M					
			Gastro	40.98 M					
			Hemato	40.98 M					
			Musc/skel	40.98 M					
			Hepatic		1.36 M (variation in nuclear size, nuclear pyknosis, extensive cytoplasmic vacuolization)				
			Renal	1.36 M (40.38 M (glycosuria, proteinuria, anisokaryosis, nuclear hyperchromicity, nuclear pyknosis, tubular atrophy)				
			Endocr	40.98 M					
Bd Wt	40.98 M								
Other	40.98 M								
Neurological									
54	Rat (Sprague-Dawley)	3 mo ad lib (W)		22.4 M			Belles et al. 2005 Uranyl Acetate	NOAEL is for behavioral effects.	
55	Rat (Sprague-Dawley)	1.5 mo ad lib (W)			2 M (cholinergic alterations in the brain)		Bensoussan et al. 2009 Uranyl Nitrate		

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					Less Serious (mg/kg/day)	Serious (mg/kg/day)		
56	Rat (Long-Evans)	6 mo ad lib (W)		14 M	28 M (increased motor activity)		Briner and Murray 2005 Depleted uranyl acetate	
57	Rat (Sprague-Dawley)	9 mo ad lib (W)			2.7 M (altered neurotransmitter levels in the brain)		Bussy et al. 2006 Depleted uranyl nitrate	
58	Rat (Sprague-Dawley)	1.5 mo ad lib (W)			2.7 (sleep and behavioral alterations)		Houpert et al. 2005 Enriched Uranyl Nitrate	
59	Rat (Sprague-Dawley)	1.5 mo ad lib (W)		2.7			Houpert et al. 2005 Depleted uranyl nitrate	
60	Rat (Sprague-Dawley)	9 mo ad lib (W)			2.5 M (decreased spatial working memory)		Houpert et al. 2007b Enriched Uranyl Nitrate	
61	Rat (Sprague-Dawley)	90 days (W)			3.7 M (increase in REM sleep)		Lestaevel et al. 2005a Depleted uranyl nitrate	
62	Rat (Sprague-Dawley)	90 d ad lib (W)			5.6 M (increased oxidative stress in brain areas).		Linares et al. 2007 Uranyl Acetate	

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				NOAEL (mg/kg/day)	Less Serious (mg/kg/day)		
Reproductive							
63	Rat (Sprague- Dawley)	28 d (W)		35.3 M 40 F			Gilman et al. 1998a Uranyl Nitrate
64	Rat (Sprague- Dawley)	91 d (W)		36.73 M 53.56 F			Gilman et al. 1998a Uranyl Nitrate
65	Rat (Sprague- Dawley)	9 mo ad lib (W)		1.9 M			Grignard et al. 2008 Depleted uranyl nitrate NOAEL is for blood levels of testosterone and 17B-estradiol.
66	Rat (Sprague- Dawley)	9 mo ad lib (W)			1.9 M (3-fold increase in plasma testosterone)		Grignard et al. 2008 Enriched Uranyl Nitrate
67	Rat (Sprague- Dawley)	3 months ad lib (W)		5.6 M	11.2 M (reduced pregnancy rate)		Linares et al. 2005 Uranyl Acetate
68	Mouse (C57BL/6N)	15 wk ad lib (W)			1.25 F (slight disturbance in ovarian folliculogenesis)		Arnault et al. 2008 Uranyl Nitrate

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					Less Serious (mg/kg/day)	Serious (mg/kg/day)		
69	Mouse (Hybrid)	49 d ad lib (W)		1.9 F	3.9 F (increased proportion of morphologically abnormal oocytes)		Feugier et al. 2008 Uranyl Nitrate	
70	Mouse (Swiss-Webster)	40 d ad lib (W)			2.5 F (increased oocyte dysmorphism and micronuclei in cumulus cells)		Kundt et al. 2009 Uranyl Nitrate	
71	Mouse (Swiss-Webster)	64 d (W)			5.6 M (significantly reduced pregnancy rate)		Llobet et al. 1991 Uranyl Acetate	
72	Mouse (Swiss-Webster)	60 d (G)		14			Paternain et al. 1989 Uranyl Acetate	NOAEL is for fertility.
73	Rabbit (New Zealand)	91 d (W)		28.7 M 43.02 F			Gilman et al. 1998b Uranyl Nitrate	
Developmental								
74	Rat (Sprague-Dawley)	132 d (W)			4.3 F (delayed hyperactivity; decreased spatial working memory)		Houpert et al. 2007a Enriched Uranyl Nitrate	

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					Less Serious (mg/kg/day)	Serious (mg/kg/day)			
75	Rat (Sprague-Dawley)	70 d ad lib (W)			22.5	(13-16% reduction in pups weight on day 21)		Sanchez et al. 2006 Uranyl Acetate	
76	Mouse (C57BL/6N)	15 wk ad lib (W)			1.25 F	(slight disturbance in ovarian folliculogenesis)		Arnault et al. 2008 Uranyl Nitrate	
77	Mouse (Swiss-Webster)	30 d 1x/d (G)					28	(decrease in litter size on PND 21; decreased day 21 viability index)	Domingo et al. 1989b Uranyl Acetate
78	Mouse (Swiss-Webster)	27 d (G)		5.6 F			14 F	(increased late resorptions and decreased live fetuses)	Paternain et al. 1989 Uranyl Acetate
79	Mouse (Swiss-Webster)	56 d (G)			2.8 F	(reduced pup's weight on PND 21)	5.6 F	(increased neonatal death per litter)	Paternain et al. 1989 Uranyl Acetate
CHRONIC EXPOSURE									
Death									
80	Rat (NS)	2 yr (F)					270	(50% mortality within first year)	Maynard and Hodge 1949; Maynard et al. 1953 Uranyl Fluoride

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					Less Serious (mg/kg/day)	Serious (mg/kg/day)		
81	Rat (NS)	2 yr (F)					660 M (70% mortality after 20 months)	Maynard and Hodge 1949; Maynard et al. 1953 Uranyl Nitrate
Systemic								
82	Rat (NS)	2 yr (F)	Resp	660				Maynard and Hodge 1949; Maynard et al. 1953 Uranyl Nitrate
			Cardio	660				
			Gastro	660				
			Hemato	170 F	330 F	(slight decr RBCs and hemoglobin)		
			Hepatic	660				
			Renal	33	170	(minimal renal tubular damage)		
			Endocr	660				
			Bd Wt	170 M	330 M	(11% decr BW gain)		

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					Less Serious (mg/kg/day)	Serious (mg/kg/day)		
83	Rat (NS)	2 yr (F)	Resp	270			Maynard and Hodge 1949; Maynard et al. 1953 Uranyl Fluoride	
			Cardio	270				
			Gastro	270				
			Hemato	81 M	140 M (decr RBC and hemoglobin; incr WBC)			
			Hepatic	270				
			Renal	54	81 (minimal tubular alterations)			
			Endocr	270				
			Bd Wt	81	140 (11-15% decr BW gain)	270 (28-30% decrease in BW gain)		

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				NOAEL (mg/kg/day)	Less Serious (mg/kg/day)		
84	Rat (NS)	2 yr (F)	Resp	12000			Maynard and Hodge 1949; Maynard et al. 1953 Uranium Dioxide
			Cardio	12000			
			Gastro	12000			
			Hemato	12000			
			Hepatic	12000			
			Renal	12000			
			Endocr	12000			
			Bd Wt	12000			
85	Rat (NS)	2 yr (F)	Resp	11000			Maynard and Hodge 1949; Maynard et al. 1953 Uranium Tetrafluoride
			Cardio	11000			
			Gastro	11000			
			Hemato	11000			
			Hepatic	11000			
			Renal	1100	11000	(mild renal tubular degeneration)	
Endocr	11000						

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					Less Serious (mg/kg/day)	Serious (mg/kg/day)		

			Bd Wt	1100	11000	(10% decr BW gain after 1 year)		
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a The number corresponds to entries in Figure 3-2.

b Used to derive an acute-duration oral minimal risk level (MRL) of 0.002 mg/kg/day for soluble uranium compounds based on a BMDL0.05 of 0.20 mg/kg/day and an uncertainty factor of 100 (10 for extrapolation from animals to humans and 10 for human variability).

c Used to derive an intermediate-duration oral minimal risk level (MRL) of 0.0002 mg/kg/day for soluble uranium compounds based on a LOAEL of 0.06 mg/kg/day and an uncertainty factor of 300 (3 for use of a minimal LOAEL, 10 for extrapolation from animals to humans and 10 for human variability).

ad lib = ad libitum; Bd Wt = body weight; Cardio = cardiovascular; d = day(s); Endocr = endocrine; (F) = feed; F = Female; (G) = gavage; Gastro = gastrointestinal; Gd = gestation day; (GW) = gavage in water; Hemato = hematological; LD50 = lethal dose, 50% kill; LOAEL = lowest-observed-adverse-effect level; M = male; Metab = metabolic; mo = month(s); Musc/skel = musculoskeletal; NOAEL = no-observed-adverse-effect level; NS = not specified; PND = post-natal day; Resp = respiratory; (W) = drinking water; wk = week(s); x = time(s); yr = year(s)