Supplementary Tables

Supplementary Table S1. Chemicals that have been found to have carcinogenic effects from prenatal or postnatal exposure in animals as identified in different review articles.

	Review articles including prenatal and postnatal exposure						
Chemical Name	**(Fujii 1991)**	**McClain et al., 2001**	**Anderson et al., 2000**	**Della Porta and Terracini, 1969**	**Druckrey 1973**	**Other Literature**	**Chemicals selected for quantitative analysis or reason for exclusion**
4-Acetylaminobiphenyl (AAB)	X						a
4-Aminoazobenzene(AB)	X						a
3-Amino-1,4,-dimethyl-5H-pyrido[4,3-b]indole (Trp-P-1)	X						a
2-Aminodipyridol[1,2-a:3',2'-d]imidazole (Glu-P-2)	X						a
2-Amino-6-methyldipyridol[1,2-a:3',2'-d]imidazole (Glu-P-1)	X						a
3-Amino-1-methyl-5H-pyrido[4,3-b]indole (Trp-P-2)	X						a
Amitrole						X	selected
Arsenic						X	a
5-Azacytidine			X				a
3'-azido-3'-deoxythymidine (AZT)			X				a
Azoxymethane					X		a
Benz(a)anthracene				X			a
Benzidine			X				selected
Benzo(a)pyrene (B[a]P)	X			X			selected
1-(4'Bromophenylazo)-1-phenyl-1-hydroperoxymethane(BPH)	X						a
N-Butyl-N-(3-carboxypropyl)nitrosamine (BCPN)	X						a
N-Butyl-N-(3 hydroxbutyl)nitrosamine (BBN)	X						a
Butylnitrosourea (BNU)	X						a
Cyclophosphamide		X					a
Dibenz[a,h]anthracene				X			selected
Dibutylnitrosamine (DBN)	X						a
Dichlorodiphenyltrichloroethane (DDT)						X	selected
Dieldrin						X	selected
2-Diethylaminoethyl-2,2-dephenylvalerate hydrochloride (SKF 525A)	X						a
Diethylnitrosamine (DEN)	X		X				selected
Diethylstilbesterol (DES)			X				a

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Chemical Name	Review articles including prenatal and postnatal exposure (Fujii 1991)	McClain et al., 2001	Anderson et al., 2000	Della Porta and Terracini, 1969	Druckrey 1973	Other Literature	Chemicals selected for quantitative analysis or reason for exclusion
4-Amino-2',3-dimethylazobenzene				X			
1,2-Dimethylhydrazine (DMH)	X						a
7,12-Dimethylbenz[a]anthracene (DMBA)	X		X	X			selected
Dimethylnitrosamine (DMN)	X		X	X			selected
5',5'-Diphenylhydantoin DPH)							selected
Estradiol	X	X					a
6-Ethoxy-2,2,4-trimethyl-1,2-dihydroquinoline (Santoquin)	X						a
Ethylene thiourea (ETU)						X	selected
Ethyl methane sulphonate				X			a
Ethylnitrosobiuret					X		a
Ethylnitrosourea (ENU)			X				selected
N-2-Fluorenylacetamide (FAA)	X			X			a
Genistein						X	a
3-Hydroxyl-4-acetylaminobiphenyl (N-OH-AAB)	X						a
N-2-hydroxy-N-2-fluorenylacetamide (N-OH-FAA)	X						a
2-Hydroxypropyl-propylnitrosamine			X				a
9-Methylanthracene				X			a
Methyl-2-benzylhydrazine			X				a
Methylcholanthrene			X	X			selected
3-Methyl-4-dimethylaminoabenzene(3'ME-DAB)	X						a
4-(Methylnitrosoamino)-1-(3-pyridyl)-1-butanone (NNK)			X				a
Methylnitrosourea (MNU)			X				selected
Methylnitrosourethane			X				a
1-Methyl-3-nitro-1-nitrosoguanidine (MNNG)	X						a
2-Naphthylamine				X			a
2-Naphthylhydroxyamine				X			a
Nickel acetate			X				a
N-Nitrosobuylamine			X				a
4-Nitroquinoline-1-oxide				X	X		a
N-Nitrosomethyl(2-oxopropyl)amine			X				a

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Chemical Name	Review articles including prenatal and postnatal exposure						Chemicals selected for quantitative analysis or reason for exclusion
	(Fujii 1991)	McClain et al., 2001	Anderson et al., 2000	Della Porta and Terracini, 1969	Druckrey 1973	Other Literature	
2-Oxopropyl-propylnitrosamine			X				a
1-Phenyl-3,3',-dimethylhydrazine					X		a
1-Phenyl-3,3,-dimethyltriazene			X				a
Polybrominated biphenyls						X	selected
Safrole (3,4-Methylenedioxyally benzene)	X		X				selected
Soot	X						a
Sterigmatocystin	X						a
Tamoxofen						X	b
1,3,5-Trimethyl-2,4,6-tris[3,5-di-tert-butyl-4-hydroxybenzyl)benzene (Ionox 33)	X						a
Urethane (Ethyl carbamate)			X	X			selected
Vinyl chloride						X	selected

a. Chemicals with juvenile studies without comparable adult studies and could not be used for the quantitative analysis based on the selection criteria
b. Incomplete study design, such as lack of controls and differing followup times

Supplementary Table S2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult multiple exposures.

Chemical	Species, Strain	Target Site	Age when first dosed	Dose Route, # doses	Dose	Duration of exposure	Age at Death	Tumors[i]		Comments	Reference
								M	F		
Amitrole	Mice ($B6C3F_1$)	Liver	Control	None	Control: 0 ppm	N/A	90 weeks	1/98 (1%)	0/96 (0%)	Incidences are mice with adenomas or carcinomas.	Vesselinovitch, 1983
			Gestation day 12	Diet, to mothers	500 ppm	Gestation day 12 to delivery		6/74 (8%)[c]	0/83 (0%)[c]		
			Newborn	Diet, to mothers	500 ppm	Birth until weaning		10/45 (22%)[c]	0/55 (0%)[c]		
			At weaning	Diet, to offspring	500 ppm	From weaning to 90 weeks		20/55 (36%)[c]	9/49 (18%)[c]		
Benzidine	Mice ($B6C3F_1$)	Liver	Control	None	Control: 0 ppm	N/A	90 weeks	1/98 (1%)	0/100 (0%)	Higher sensitivity in males during perinatal period, in females during adulthood. Incidences are mice with adenomas or carcinomas.	Vesselinovitch et al., 1975b; Vesselinovitch et al., 1979a
			Gestation day 12	Diet, to mothers	150 ppm	Gestation day 12 to delivery		17/55 (31%)[a]	2/62 (3%)[b]		
			Newborn	Diet, to mothers	150 ppm	Birth until weaning		62/65 (95%)[a]	2/43 (5%)[b]		
			At weaning	Diet, to offspring	150 ppm	From weaning to 90 weeks		22/50 (44%)[a]	47/50 (94%)[a]		
			Gestation day 12	Diet, to mothers	150 ppm	Gestation day 12 until weaning		49/49 (100%)[a]	12/48 (25%)[a]		
			Gestation day 12	Diet, to mothers	150 ppm	Gestation day 12 until 90 weeks		50/50 (100%)[a]	47/50 (94%)[a]		

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a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

[i] Where not delineated by gender, data combined by study authors or gender not specified. Where percentages only are given, number of subjects not specified.

Chemical	Species, Strain	Target site	Age when first dosed	Dose Route, # doses	Dose	Duration of exposure	Age at death	Tumors		Comments	Reference
								M	F		
DDT Dichlorodiphenyltrichloroethane	Mice (B6C3F1)	Liver	Control	None	Control: 0 ppm	N/A	90 weeks	1/50 (2%)	-		Vesselinovitch et al., 1979b
			Week 1	Gavage, daily	230 µg	Weeks 1-4		5/49 (10%)[b]	-		
			Week 5	Diet, daily	150 ppm	Weeks 5-90		8/49 (16%)[b]	-		
			Week 1	Gavage, daily until 4 weeks, then in diet	230 µg 150 ppm (diet)	Weeks 1-90		10/50 (20%)[a]	-		
Dieldrin	Mice (B6C3F1)	Liver	Control	None	Control: 0 ppm	N/A	90 weeks	1/58 (2%)	-		Vesselinovitch et al., 1979b
			Week 1	Gavage, daily	12.5 µg	Week 1-4		3/46 (7%)[b]	-		
			Week 5	Diet, daily	10 ppm	Weeks 5-90		7/60 (12%)[b]	-		
			Week 1	Gavage, daily until 4 weeks, then in diet	12.5 µg 10 ppm	Weeks 1-90		21/70 (30%)[a]	-		

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Chemical	Species, Strain	Target site	Age when first dosed	Dose Route, # doses	Dose	Duration of exposure	Age at Death	Tumors M	Tumors F	Comments	Reference
DEN[ii] Diethylnitrosamine	Rats (Colworth)	Liver	Control		Control	N/A		29/384 (8%)		Highest tumor rate when dosed at earlier ages. Incidents are rats with adenomas or carcinomas	Peto et al., 1984
			Week 3	Diet (in drinking water), daily	16 different doses combined[iii]	From week 3 until death	6 months-3 years	105/180 (58%)[c]			
			Week 6			From week 6 until death		714/1440 (50%)[c]			
			Week 20			From week 20 until death		76/180 (42%)[c]			
		Esophagus	Control		Control	N/A		0/384 ()%)			
			Week 3	Diet (in drinking water), daily	16 different doses combined[iv]	From week 3 until death		77/180 (43%)[c]			
			Week 6			From week 6 until death		663/1440 (46%)[c]			
			Week 20			From week 20 until death		88/180 (49%)[c]			

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a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

[ii] Reported as NDEA (N-nitrosodiethylamine) in the original document.
[iii] Results from each dose are not available.
[iv] Results from each dose are not available.

Chemical	Specie, Strain	Target site	Age when first dosed	Dose Route, # doses	Dose	Duration of exposure	Age at death	Tumors		Comments	Reference
								M	F		
DPH Diphenylhydantoin, 5,5-	Rats (F344/N)	Liver	Control	Control	0 ppm	N/A	2 years	0/50 (0%)	0/50 (0%)	In rats, perinatal exposure ranged from 63-630 ppm, and adult rat exposures ranged from 240-2400 ppm. In mice, perinatal exposure ranged from 21 to 210 ppm. Adult exposure ranged from 30-300 ppm in males and 60-600 ppm in females. Tumor incidences are animals with adenomas or carcinomas.	Chhabra et al., 1993b
			Perinatal	Diet, daily	630 ppm	Perinatal through 8 weeks		1/50 (2%)[b]	0/49 (0%)[b]		
			8 weeks		800 ppm	8 weeks – 2 years		2/50 (4%)[b]	1/50 (2%)[b]		
			8 weeks		2400 ppm	8 weeks – 2 years		4/50 (8%)[b]	1/50 (2%)[b]		
			Perinatal		630-800	Perinatal through 2 years		1/49 (2%)[b]	0/50 (0%)[b]		
			Perinatal		630-2400 ppm	Perinatal through 2 years		5/49 (10%)[a]	0/50 (0%)[b]		
	Mice ($B6C3F_1$)	Liver	Control	Control male	0 ppm	N/A	2 years	29/50 (58%)			
			Perinatal	Diet, male	210 ppm	Perinatal through 8 weeks		33/50 (66%)[b]			
			8 weeks		100 ppm	8 weeks – 2 years		29/49 (59%)[b]			
			8 weeks		300 ppm	8 weeks – 2 years		26/49 (53%)[b]			
			Perinatal		210-100 ppm	Perinatal through 2 years		35/49 (71%)[b]			
			Perinatal		210-300 ppm	Perinatal through 2 years		41/50 (82%)[a]			
			Control	Control female	0 ppm	N/A	2 years		5/48 (10.4%)[b]		
			Perinatal	Diet, female	210 ppm	Perinatal through 8 weeks			12/49 (24.5%)[b]		
			8 weeks		200 ppm	8 weeks – 2 years			14/49 (28%)[a]		
			8 weeks		600 ppm	8 weeks – 2 years			30/50 (60%)[a]		
			Perinatal		210-200 ppm	Perinatal through 2 years			16/50 (32%)[a]		
			Perinatal		210-600 ppm	Perinatal through 2 years			34/50 (68%)[a]		

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Chemical	Species, Strain	Target site	Age when first dosed	Dose Route, # doses	Dose	Duration of exposure	Age at death	Tumors		Comments	Reference
								M	F		
ETU Ethylene thiourea	Rats (F344/N)	Thyroid	Control	Control	0 ppm	N/A	2 years	1/49 (2%)	3/50 (6%)	Tumor incidences are animals with adenomas or carcinomas.	Chhabra et al., 1992
			Perinatal	Diet, daily	90 ppm	Perinatal through 8 weeks		4/49 (8%)[b]	3/50 (6%)[b]		
			8 weeks		83 ppm	8 weeks – 2 years		12/46 (26%)[a]	7/44 (16%)[b]		
			8 weeks		250 ppm	8 weeks – 2 years		37/50 (74%)[a]	30/49 (61%)[a]		
			Perinatal		90-83 ppm	Perinatal through 2 years		13/50 (26%)[a]	9/47 (19%)[b]		
			Perinatal		90-250 ppm	Perinatal through 2 years		48/50 (96%)	37/50 (74%)		
	Mice ($B6C3F_1$)	Liver	Control	Control	0 ppm	N/A	2 years	20/49 (41%)	4/50 (8%)		
			Perinatal	Diet, daily	330 ppm	Perinatal through 8 weeks		13/49 (26.5%)[b]	5/49 (10%)[b]		
			8 weeks		330 ppm	8 weeks – 2 years		32/50 (64%)[a]	44/50 (88%)[a]		
			8 weeks		1000 ppm	8 weeks – 2 years		46/50 (92%)[a]	48/50 (96%)[a]		
			Perinatal		330-330 ppm	Perinatal through 2 years		34/49 (69%)[a]	46/50 (92%)[a]		
			Perinatal		330-1000 ppm	Perinatal through 2 years		47/49 ((6%)[a]	49/50 (98%)[a]		
		Thyroid	Control	Control	0 ppm	N/A		1/50 (2%)	0/50 (0%)		
			Perinatal	Diet, daily	330 ppm	Perinatal through 8 weeks		1/46 (2%)[b]	1/49 (2%)[b]		
			8 weeks		330 ppm	8 weeks – 2 years		1/49 (2%)[b]	2/50 (4%)[b]		
			8 weeks		1000 ppm	8 weeks – 2 years		29/50 (58%)[a]	38/50 (76%)[a]		
			Perinatal		330-330 ppm	Perinatal through 2 years		2/48 (4%)[b]	10/49 (20%)[a]		
			Perinatal		330-1000 ppm	Perinatal through 2 years		35/49 (71%)[a]	38/50 (76%)[a]		

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Chemical	Species, Strain	Target site	Age when first dosed	Dose Route, # doses	Dose	Duration of exposure	Age at death	Tumors		Comments	Reference
								M	F		
ETU Ethylene thiourea	Mice ($B6C3F_1$)	Pituitary	Control	Control	0 ppm	N/A	2 years (cont.)	0/44 (0%)	11/47 (23%)	Tumor incidences are animals with adenomas or carcinomas.	Chhabra et al., 1992
			Perinatal	Diet, daily	330 ppm	Perinatal through 8 weeks		0/42 (0%)[b]	11/48 (23%)[b]		
			8 weeks		330 ppm	8 weeks – 2 years		0/42 (0%)[b]	19/49 (39%)[b]		
			8 weeks		1000 ppm	8 weeks – 2 years		8/41 (19.5%)[a]	26/49 (53%)[a]		
			Perinatal		330-330 ppm	Perinatal through 2 years		0/45 (0%)[b]	26/47 (55%)[a]		
			Perinatal		330-1000 ppm	Perinatal through 2 years		4/39 (10%)[b]	24/47 (51%)[a]		

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a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

Chemical	Species, Strain	Target Site	Age when first dosed	Dose Route, # doses	Dose	Duration of exposure	Age at death		Tumor Incidence		Reference
							M	F	M	F	
3-Methylcholanthrene (formerly known as 20-Methylcholanthrene)	Mice (Albino)	Liver	Control	gavage,3X per week	NA	NA	475 days	480 days	3/39 (7.7%)	0/36 (0%)	Klein, 1959
			8 days		0.25 mg/g	10X	311 days	321 days	21/25 (84%) [c]	7/30 (23.3%) [c]	
			90 days		0.25 mg/g	10X	330 days	366 days	1/26 (3.8%) [c]	0/29 (0%) [b]	
		Lung	Control		NA	NA	475 days	480 days	17/39 (43.6%)	14/36 (38.9%)	
			8 days		0.25 mg/g	10X	311 days	321 days	25/25 (100%) [c]	28/30 (93.3%) [c]	
			90 days		0.25 mg/g	10X	330 days	366 days	25/26 (96.2%) [c]	27/29 (93.1%) [c]	
		Fore-stomach	Control		NA	NA	475 days	480 days	0/39 (0%)	0/36 (0%)	
			8 days		0.25 mg/g	10X	311 days	321 days	12/25 (48%) [c]	12/30 (40%) [c]	
			90 days		0.25 mg/g	10X	330 days	366 days	13/26 (50%) [c]	8/29 (27.6%) [c]	
		Skin	Control		NA	NA	475 days	480 days	0/39 (0%)	0/36 (0%)	
			8 days		0.25 mg/g	10X	311 days	321 days	4/25 (16%) [c]	4/30 (13.3%) [c]	
			90 days		0.25 mg/g	10X	330 days	366 days	1/26 (3.8%) [c]	1/25 (4%) [c]	

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a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

Chemical	Species, Strain	Target site	Age when first dosed	Dose Route, # Doses	Dose	Duration of exposure	Age at death	Tumors		Comments	Reference
								M	F		
PBBs Polybrominated biphenyls	Rats (F344/N)	Liver[v]	Control	Control	0 ppm	N/A	2 years	1/50 (2%)	0/50 (0%)	Findings suggest that combined perinatal and adult exposure increases PBB-related hepatocellular carcinogenicity relative to adult-only exposure in mice and female rats. Apparent association between increasing incidences of MCL and exposure to PBB in male and female rats. Tumor incidences are animals with adenomas or carcinomas	Chhabra et al., 1993a
			Perinatal	Diet	10 ppm	Perinatal – 8 weeks		5/50 (10%)[b]	0/50 (0%)[b]		
			8 weeks		10 ppm	8 weeks – 2 years		12/49 (24%)[a]	12/50 (24%)[a]		
			8 weeks		30 ppm	8 weeks – 2 years		41/50 (82%)[a]	39/50 (78%)[a]		
			Perinatal		10-10 ppm	Perinatal – 2 years		16/50 (32%)[a]	39/50 (78%)[a]		
			Perinatal		10-30 ppm	Perinatal – 2 years		41/50 (82%)[a]	47/50 (94%)[a]		
		Mononuclear cell leukemia (MCL)	Control	Control	0 ppm	N/A	2 years	25/50 (50%)	14/50 (28%)		
			Perinatal	Diet	10 ppm	Perinatal – 8 weeks		31/50 (62%)[b]	13/50 (26%)[b]		
			8 weeks		10 ppm	8 weeks – 2 years		33/50 (66%)[a]	22/50 (44%)[b]		
			8 weeks		30 ppm	8 weeks – 2 years		31/50 (62%)[b]	23/50 (46%)[a]		
			Perinatal		10-10 ppm	Perinatal – 2 years		37/50 (74%)[a]	27/50 (54%)[a]		
			Perinatal		10-30 ppm	Perinatal – 2 years		37/50 (74%)[a]	25/50 (50%)[a]		
	Mice ($B6C3F_1$)	Liver[vi]	Control	Control	0 ppm	N/A	2 years	16/50 (32%)	5/50 (10%)		
			Perinatal	Diet	30 ppm	Perinatal – 8 weeks		40/50 (80%)[a]	21/50 (42%)[a]		
			8 weeks		10 ppm	8 weeks – 2 years		48/49 (98%)[a]	42/50 (84%)[a]		
			8 weeks		30 ppm	8 weeks – 2 years		48/50 (96%)[a]	47/48 (98%)[a]		
			Perinatal		10 ppm	Perinatal – 2 years		46/49 (94%)[a]	44/50 (88%)[a]		
			Perinatal		30-30 ppm	Perinatal – 2 years		50/50 (100%)[a]	47/47 (100%)[a]		

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a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

[v] Tumors were adenomas or carcinomas.
[vi] Tumors were adenomas or carcinomas.

Chemical	Species, Strain	Target site	Age when first dosed	Dose Route, # Doses	Dose	Duration of exposure	Age at death	Tumors		Comments	Reference
								M	F		
Safrole	Mice ($B6C3F_1$)	Liver	Control	None	None	N/A	90 weeks	3/100 (3%)	0/100 (0%)	Highest tumor rate in males due to preweaning treatment. Highest tumor rate in females due to susceptibility in adulthood. Tumor incidences ae mice with adenomas or carcinomas.	Vesselinovitch et al., 1979b
			Day 12 of gestation	Gavage, to mothers	120 µg/g body weight	4x (days 12, 14, 16, 18)		2/61 (3%)[b]	0/65 (0%)[b]		
			Newborn	Gavage, to mothers, on alternate days	120 µg/g body weight	From birth until weaning		28/83 (34%)[a]	2/80 (3%)[b]		
			At weaning	Gavage, to offspring, 2x weekly	120 µg/g body weight	From weaning until 90 weeks		4/35 (11%)[b]	22/36 (61%)[a]		
			Day 12 of gestation	Gavage, to mothers, alternate days	120 µg/g body weight	From gestation until weaning		22/68 (32%)[c]	1/72 (1%)[c]		
			Day 12 of gestation	Gavage, to mothers, alternate days until weaning; Gavage, to offspring, 2x weekly	120 µg/g body weight	From gestation until 90 weeks		19/37 (51%)[c]	37/46 (80%)[c]		
Urethane	Mice (B6AF1/J)	Liver	1 week	gavage	2.5 mg/pup	1x	39-40 weeks	12/37 (33%)[c]	0/40 (0%)[c]	No tumor data for controls	Klein, 1966
			1 week		2.5 mg/pup	16x (1x at 1 week; 3x weekly for 5 weeks beginning at 4 wks of age)	39 weeks	11/33 (33%)[c]	0/31 (0%)[c]		
			4 weeks		2.5 mg/pup	15x (3x weekly for 5 weeks beginning at 4 weeks of age)	41 weeks	0/37 (0%)[c]	0/31 (0%)[c]		

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a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

Chemical	Species, Strain	Target site	Age when first dosed	Dose Route, # Doses	Dose	Duration of exposure	Age at death	Tumors		Comments	Reference
								M	F		
VC Vinyl Chloride	Rats (Sprague-Dawley)	Liver angio-sarcoma	Control	Control	0 ppm	N/A	135 weeks	0/22 (0%)	0/29 (0%)	Higher tumor risk when exposed at birth, higher for females.	Maltoni et al., 1984
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk, 5 weeks	124 weeks	5/18 (28%)[c]	12/24 (50%)[c]		
					10,000 ppm			6/24 (25%)[c]	9/20 (45%)[c]		
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk, 52 weeks	135 weeks	3/17 (18%)[c]	10/25 (40%)[c]		
					10,000 ppm			3/21 (14%)[c]	4/25 (16%)[c]		
		Zymbal gland	Control	Control	0 ppm	N/A	135 weeks	0/28 (0%)	0/29 (0%)		
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk, 5 weeks	124 weeks	1/12 (8%)[c]	1/17 (6%)[c]		
					10,000 ppm			1/17 (6%)[c]	0/17 (0%)[c]		
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk, 52 weeks	135 weeks	3/29 (10%)[c]	4/30 (13%)[c]		
					10,000 ppm			10/30 (33%)[c]	6/30 (20%)[c]		
		Leukemia	Control	Control	0 ppm	N/A	135 weeks	0/27 (0%)	1/29 (3%)		
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk, 5 weeks	124 weeks	N/A	1/7 (14%)[c]		
					10,000 ppm			2/6 (33%)[c]	0/15 (0%)[c]		
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk, 52 weeks	135 weeks	N/A	0/29 (0%)[c]		
					10,000 ppm			0/27 (0%)[c]	2/29 (7%)[c]		
		Nephro-blastoma	Control	Control	0 ppm	N/A	135 weeks	0/22 (0%)	0/29 (0%)		
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk, 5 weeks	124 weeks	0/15 (0%)[c]	0/21 (0%)[c]		
					10,000 ppm			0/19 (0%)[c]	0/17 (0%)[c]		
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk, 52 weeks	135 weeks	4/18 (22%)[c]	1/26 (4%)[c]		
					10,000 ppm			3/21 (14%)[c]	2/25 (8%)[c]		
		Angio-sarcomas: other sites	Control	Control	0 ppm	N/A	135 weeks	0/29 (0%)	0/29 (0%)		

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Chemical	Species, Strain	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors M	Tumors F	Comments	Reference
VC Vinyl Chloride	Rats (Sprague-Dawley	Angio-sarcomas: other sites	Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk,	124 weeks	1/15 (7%)[c]	0/21 (0%)[c]		Maltoni et al., 1984
					10,000 ppm	5 weeks		0/19 (0%)	0/17 (0%)[c]		
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk,	135 weeks	1/29 (3%)[c]	2/30 (7%)[c]		
					10,000 ppm	52 weeks		2/30 (7%)[c]	1/30 (3%)[c]		
		Angiomas and fibromas: other sites	Control	Control	0 ppm	N/A	135 weeks	0/28 (0%)	2/29 (7%)[c]		
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk,	124 weeks	1/15 (7%)[c]	0/21 (0%)[c]		
					10,000 ppm	5 weeks		2/19 (11%)[c]	1/17 (6%)[c]		
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk,	135 weeks	2/29 (7%)[c]	2/30 (7%)[c]		
					10,000 ppm	52 weeks		2/29 (7%)[c]	1/29 (3%)[c]		
		Hepatoma	Control	Control	0 ppm	N/A	135 weeks	0/19 (0%)	0/28 (0%)		
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk,	124 weeks	9/18 (50%)[c]	11/24 (46%)[c]		
					10,000 ppm	5 weeks		13/24 (54%)[c]	7/20 (35%)[c]		
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk,	135 weeks	0/10 (0%)[c]	1/17 (6%)[c]		
					10,000 ppm	52 weeks		1/8 (13%)[c]	0/16 (0%)[c]		
		Skin carinomas	Control	Control	0 ppm	N/A	135 weeks	0/20 (0%)	1/29 (3%)		
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk,	124 weeks	1/10 (10%)[c]	1/14 (7%)[c]		
					10,000 ppm	5 weeks		1/16 (6%)[c]	0/15 (0%)[c]		
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk,	135 weeks	0/15 (0%)[c]	2/19 (11%)[c]		
					10,000 ppm	52 weeks		2/13 (15%)[c]	1/21 (5%)[c]		
		Neuro-blastoma	Control	Control	0 ppm	N/A	135 weeks	0/22 (0%)	0/29 (0%)		
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk,	124 weeks	0/18 (0%)[c]	0/29 (0%)[c]		
					10,000 ppm	5 weeks		0/22 (0%)[c]	0/19 (0%)[c]		

Chemical	Species, Strain	Target site	Age when first dosed	Dose Route, # doses	Dose	Duration of exposure	Age at death	Tumors		Comments	Reference
								M	F		
VC Vinyl Chloride	Rats (Sprague-Dawley	Neuro-Blastoma	Week 13		6,000 ppm 10,000 ppm	4 hrs/day, 5 days/wk, 52 weeks	135 weeks	2/21 (10%)[c] 2/22 (9%)[c]	1/27 (4%)[c] 5/26 (19%)[c]		Maltoni et al., 1984

a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

Supplementary Table S3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure.

Chemical	Species, Strain	Target site	Age when first dosed	Dose Route, # doses	Dose	Duration of exposure	Age at death	Tumors[vii] M	Tumors[vii] F	Comments	Reference
Benzo(a)pyrene	Mice ($B6C3F_1$)	Liver	Control	Control	None	N/A	142 weeks	7/100 (7%)	1/100 (1%)	In general, hepatomas developed with significantly higher incidence ($p<0.01$) in mice that were treated within 24 hours of birth or at 15 days of age than they did in similarly treated animals at 42 days of age. + higher for males	Vesselinovitch et al., 1975a
			Day 1	IP[viii]	75 µg/g body weight	1x	86 weeks (m) 129 weeks (f)	26/47 (55%)[c]	3/45 (7%)[c]		
					150 µg/g body weight	1x	81 weeks (m) 121 weeks (f)	51/63 (81%)[c]	8/45 (18%)[c]		
			Day 15	IP	75 µg/g body weight	1x	93 weeks (m) 116 weeks (f)	36/60 (60%)[c]	4/55 (7%)[c]		
					150 µg/g body weight	1x	81 weeks (m) 90 weeks (f)	32/55 (58%)[c]	4/55 (7%)[c]		
			Day 42	IP	75 µg/g body weight	1x	108 weeks(m)	7/55 (13%)[c]	0/47 (0%)[c]		
					150 µg/g body weight	1x	87 weeks (m)	4/47 (9%)[c]	0/46 (0%)[c]		
Benzo(a)pyrene	Mice ($C3A\ F_1$)	Liver	Control	Control	None	N/A	142 weeks	8/100 (8%)	1/100 (1%)	+ higher for males "Age at death" is the average age at which tumors were observed.	
			Day 1	IP	75 µg/g body weight	1x	80 weeks (m) 91 weeks (f)	21/62 (34%)[c]	1/45 (2%)[c]		
					150 µg/g body weight	1x	69 weeks (m) 701 weeks (f)	24/52 (46%)[c]	1/56 (2%)[c]		
			Day 15	IP	75 µg/g body weight	1x	90 weeks (m) 102 weeks (f)	15/56 (27%)[c]	1/49 (2%)[c]		

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[vii] Where not delineated by gender, data combined by study authors or gender not specified. Where percentages only are given, number of subjects not specified.
[viii] Intraperitoneal injection (IP)

Chemical	Species, Strain	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[ix]		Comments	Reference
								M	F		
Benzo(a)pyrene	Mice ($C3A F_1$)	Liver		IP	150 µg/g body weight	1x	77 weeks (m) 62 weeks (f)	12/53 (23%)[c]	1/57 (2%)[c]		
			Day 42	IP	75 µg/g body weight	1x		0/30 (0%)[c]	0/32 (0%)[c]		
					150 µg/g body weight	1x	79 weeks (m)	1/32 (3%)[b]	0/40 (0%)[c]		
Benzo(a)pyrene	Mice ($B6C3F_1$)	Lung	Control	Control	Control	N/A	142 weeks	13/100 (13%)	9/100 (9%)	Both sexes developed lung tumors with higher incidence when treated with B(a)P at birth than at 15 or 42 days of age ($p<0.05$).	
			Day 1	IP	75 µg/g body weight	1x	103 weeks(m) 126 weeks (f)	20/47 (43%)[c]	22/45 (49%)[c]		
					150 µg/g body weight	1x	84 weeks(m) 112 weeks (f)	37/63 (59%)[c]	28/45 (62%)[c]		
			Day 15	IP	75 µg/g body weight	1x	103 weeks(m) 122 weeks (f)	15/60 (25%)[c]	18/55 (33%)[c]		
					150 µg/g body weight	1x	82 weeks(m) 101 weeks (f)	20/55 (36%)[c]	18/45 (40%)[c]		
			Day 42	IP	75 µg/g body weight	1x	119 weeks(m) 131 weeks (f)	20/55 (36%)[c]	12/47 (26%)[c]		
					150 µg/g body weight	1x	95 weeks(m) 118 weeks (f)	18/47 (38%)[c]	8/46 (17%)[c]		

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a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

[ix] Where not delineated by gender, data combined by study authors or gender not specified. Where percentages only are given, number of subjects not specified.

Chemical	Species, Strain	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors		Comments	Reference
								M	F		
Benzo(a)pyrene	Mice ($C3A F_1$)	Lung	Control	Control	None	N/A	142 weeks	60/100 (60%)	50/100 (50%)	Of the 2 mouse strains tested, C3AF1 mice developed significantly more tumors than did the B6C3F1 mice ($p<0.001$)	Vesselinovitch et al., 1975a
			Day 1	IP	75 µg/g body weight	1x	78 weeks(m) 82 weeks (f)	58/62 (93%)[c]	42/45 (93%)[c]		
					150 µg/g body weight	1x	70 weeks(m) 73 weeks (f)	48/52 (92%)[c]	52/56 (93%)[c]		
			Day 15	IP	75 µg/g body weight	1x	87 weeks(m) 98 weeks (f)	52/56 (93%)[c]	46/49 (94%)[c]		
					150 µg/g body weight	1x	75 weeks(m) 79 weeks (f)	50/53 (94%)[c]	52/57 (91%)[c]		
			Day 42	IP	75 µg/g body weight	1x	91 weeks(m) 93 weeks (f)	28/30 (93%)[c]	28/32 (87%)[c]		
					150 µg/g body weight	1x	85 weeks(m) 83 weeks (f)	28/32 (87%)[c]	36/40 (90%)[c]		
DBA Dibenzanthracene	Mice (Caracul x P stock)	Lung	Control	Control	None	N/A	228 days	1/31 (3.2%)			Law, 1940
			Day 1	IP	4 mg per cm^3 vehicle	1x	181 days	24/24 (100%)[c]			
			2 months	SC[x]	4 mg per cm^3 vehicle	1x	189 days	2/29 (6.9%)[c]			
DEN Diethylnitrosamine	Mice ($B6C3F_1$)	Liver	Control	Control	Vehicle (0.01 ml trioctanoin/g body weight)	4x	142 weeks(m) 137 weeks (f)	7/98 (7%)	1/100 (1%)	Animals treated as newborns and infants developed significantly more liver tumors than animals that were treated as young adults. Newborns and infant females developed liver tumors at a later age than similarly treated males. Incidences for malignant tumors only.	Vesselinovitch et al., 1984
			Day 1	IP (3-, 6- and 6-day intervals)	1.5 µg/g body weight	4x	67 weeks (m) 90 weeks (f)	37/51 (73%)[c]	45/64 (70%)[c]		
					3 µg/g body weight	4x	65 weeks (m) 80 weeks (f)	40/58 (69%)[c]	44/65 (68%)[c]		
			Day 15		1.5 µg/g body weight	4x	86 weeks (m) 117 weeks (f)	41/57 (72%)[c]	40/71 (56%)[c]		
					3 µg/g body weight	4x	76 weeks (m) 96 weeks (f)	48/69 (70%)[c]	46/62 (74%)[c]		
			Day 42		1.5 µg/g body weight	4x	117 weeks(m) 135 weeks (f)	9/49 (18%)[c]	1/47 (2%)[c]		
					3 µg/g body weight	4x	123 weeks(m) 133 weeks (f)	6/38 (16%)[c]	4/57 (7%)[c]		

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a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

[x] Subcutaneous injection (SC)

Chemical	Species, Strain	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors		Comments	Reference
								M	F		
DEN Diethylnitrosamine	Mice ($C3AF_1$)	Liver	Control	Control	Vehicle (0.1 trioctanoin/g body weight)	4x	123 weeks(m) 131weeks (f)	8/99 (8%)	1/97 (1%)	Highest tumor rate when dosed at early ages.	Vesselinovitch et al., 1984
			Day 1	IP (3-, 6- and 6-day intervals)	1.5 µg/g body weight	4x	64 weeks (m) 84 weeks (f)	23/32 (72%)[c]	11/39 (28%)[c]	Newborns and infant females developed liver tumors at a lower incidence than similarly treated males.	
					3 µg/g body weight	4x	59 weeks (m) 76 weeks (f)	39/58 (67%)[c]	26/50 (52%)[c]		
			Day 15		1.5 µg/g body weight	4x	82 weeks (m) 102 weeks (f)	22/46 (48%)[c]	8/65 (12%)[c]		
					3 µg/g body weight	4x	74 weeks (m) 94 weeks (f)	35/54 (65%)[c]	22/62 (35%)[c]		
			Day 42		1.5 µg/g body weight	4x	105 weeks(m) 106 weeks (f)	12/56 (22%)[c]	0/53 (0%)[c]	+ higher for males	
					3 µg/g body weight	4x	105 weeks(m) 103 weeks (f)	9/57 (16%)[c]	0/56 (0%)[c]		
	Mice ($B6C3F_1$)	Lung	Control	Control	Vehicle (0.1 trioctanoin/g body weight)	4x	142 weeks(m) 137 weeks (f)	13/98 (13%)	9/100 (9%)	The mice treated as newborns showed lung tumors earlier than animals exposed at other times. It is not known whether this was due to actual earlier emergence of tumors or to their earlier detection caused by shorter survival.	
			Day 1	IP (3-, 6- and 6-day intervals)	1.5 µg/g body weight	4x	70 weeks (m) 91 weeks (f)	29/51 (57%)[c]	49/64 (77%)[c]		
					3 µg/g body weight	4x	68 weeks (m) 81 weeks (f)	34/58 (59%)[c]	42/65 (65%)[c]		

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Chemical	Species, Strain	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors		Comments	Reference
								M	F		
	Mice ($B6C3F_1$) (cont.)	Lung (cont.)	Day 15	IP (3-,6- and 6-day intervals)	1.5 µg/g body weight	4x	87 weeks (m) 115 weeks (f)	51/57 (89%)[c]	61/71 (86%)[c]		
					3 µg/g body weight	4x	77 weeks (m) 97 weeks (f)	51/69 (74%)[c]	53/62 (85%)[c]		
			Day 42		1.5 µg/g body weight	4x	123 weeks(m) 129 weeks (f)	38/49 (78%)[c]	38/47 (81%)[c]		
					3 µg/g body weight	4x	121 weeks(m) 127 weeks (f)	33/38 (87%)[c]	43/57 (75%)[c]		
	Mice ($C3AF_1$)	Lung	Control	Control	Vehicle (0.1 trioctanoin/g body weight)	4x	142 weeks(m) 137weeks (f)	60/99 (61%)	50/97 (52%)	Of the two strains, C3AF1 mice developed lung tumors with a higher incidence and multiplicity than B6C3F1 hybrids.	
			Day 1	IP (3-, 6- and 6-day intervals)	1.5 µg/g body weight	4x	65 weeks (m) 84 weeks (f)	30/32 (94%)[c]	38/39 (97%)[c]		
					3 µg/g body weight	4x	59 weeks (m) 76 weeks (f)	49/58 (84%)[c]	46/50 (92%)[c]		
			Day 15		1.5 µg/g body weight	4x	80 weeks (m) 101 weeks (f)	42/46 (91%)[c]	61/65 (94%)[c]		
					3 µg/g body weight	4x	74 weeks (m) 92 weeks (f)	50/54 (93%)[c]	57/62 (92%)[c]		
			Day 42		1.5 µg/g body weight	4x	104 weeks(m) 110 weeks (f)	55/56 (98%)[c]	52/53 (98%)[c]		
					3 µg/g body weight	4x	101 weeks(m) 102 weeks (f)	56/57 (98%)[c]	54/56 (96%)[c]		

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a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

Chemical	Species, Strain	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors M	Tumors F	Comments	Reference
DEN Diethylnitrosamine	Mice ($B6C3F_1$)	Liver	Control	Control	None	N/A	90 weeks	1/98 (1%)	0/96 (0%)	Infant animals of both sexes (Day 15) were more sensitive than similarly exposed adults.	Vesselinovitch and Mihailovich, 1983
			Gestation day 18	IP	1.5 µg/g body weight	1x		2/50 (4%)[c]	1/51 (2%)[c]		
			Day 15	IP (3-, 6- and 6-day intervals)	1.5 µg/g body weight	4x		47/51 (92%)[c]	60/64 (94%)[c]		
			Day 42		1.5 µg/g body weight	4x		13/49 (26%)[c]	3/47 (6%)[c]		
			Day 1	IP	1.5 µg/g body weight	1x	73 weeks	15/59 (25%)[c]	-	At the 1.5 µg dose level, 1-day-old mice developed significantly fewer liver tumors than similarly treated infants (Day 15) ($p<0.025$). Tumor incidence in treated groups versus controls was not evaluated.	Vesselinovitch et al., 1979a
					5 µg/g body weight	1x		29/45 (64%)[c]	-		
					10 µg/g body weight	1x		24/25 (96%)[c]	-		
			Day 15	IP	1.5 µg/g body weight	1x		13/24 (54%)[c]	-		
					5 µg/g body weight	1x		40/54 (74%)[c]	-		
					10 µg/g body weight	1x		25/25 (100%)[c]	-		
DMBA Dimethyl-benz(a)anthracene	Rats (Sprague-Dawley)	Mammary adeno-sarcoma	Day 20	Gavage	10 mg/100 g body weight	1x	Week 25	-	3/6 (50%)[c]	36 of 42 (86%) animals dosed at age 20 days died soon after. Highest number of tumors per animal was in the 46-day group, with decreasing numbers in the older animals. Animals were sacrificed 22 weeks after treatment.	Russo et al., 1979
			Day 30		10 mg/100 g body weight	1x	Week 26	-	14/15 (93%)[c]		
			Day 40		10 mg/100 g body weight	1x	Week 27	-	8/9 (89%)[c]		
			Day 46		10 mg/100 g body weight	1x	Week 28	-	8/8 (100%)[c]		
			Day 55		10 mg/100 g body weight	1x	Week 29	-	33/34 (97%)[c]		
			Day 70		10 mg/100 g body weight	1x	Week 32	-	5/8 (63%)[c]		
			Day 140		10 mg/100 g body weight	1x	Week 42	-	10/15 (67%)[c]		
			Day 180		10 mg/100 g body weight	1x	Week 47	-	14/26 (54%)[c]		

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a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

Chemical	Species, Strain	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors M	Tumors F	Comments	Reference
DMBA Dimethyl-benz(a)anthracene	Rats (Wistar)	Mammary carcinoma[xi]	Control 5-8 weeks	Control	None	N/A	17 months	0/22 (0%)	0/25 (0%)	Highest tumor rate in females exposed at 5-8 weeks. Animals were observed for 16 months following treatment.	Meranze et al., 1969
			Control 26 weeks	Control	None	N/A	20 months	0/31 (0%)	2/20 (10%)		
			< Week 2	Gavage	0.5-1.0 mg	1x	Week 40-56	0/23 (0%)[c]	4/50 (8%)[c]		
			Week 5-8		15 mg	1x	Week 14-55	0/23 (0%)[c]	14/25 (56%)[c]		
			Week 26		15 mg	1x	Week 32-73	0/34 (0%)[c]	4/26 (15%)[c]		
	Rats (Wistar, castrated)	Mammary carcinoma	Week 5-8	Gavage	15 mg	1x	Week 14-55	0/21 (0%)[c]	0/22 (0%)[c]		
			Week 26		15 mg	1x	Week 32-73	0/33 (0%)[c]	0/26 (0%)[c]		
	Rats (Wistar)	Total tumors	Control 5-8 weeks	Control	None	N/A	17 months	0/22 (0%)	0/25 (0%)	Total tumors includes leukemia.	
			Control 26 weeks	Control	None	N/A	20 months	2/31 (6%)	5/20 (25%)		
			< Week 2	Gavage	0.5-1.0 mg	1x	Week 40-56	16/23 (70%)[c]	36/50 (72%)[c]		
			Week 5-8		15 mg	1x	Week 14-55	7/23 (30%)[c]	16/25 (64%)[c]		
			Week 26		15 mg	1x	Week 32-73	12/34 (35%)[c]	13/26 (50%)[c]		
	Mice (BALB/c)	Lung	Control: Day 1	Control SC	Aqueous gelatine	1x	40 weeks	0/12 (0%)	7/23 (30%)	15 µg DMBA gave rise to a significantly greater incidence of lung tumors when administered to newborn mice than to suckling or young adults.	Walters, 1966
			Day 1	SC	15 µg	1x	40 weeks[xii]	14/14 (100%)[c]	24/24 (100%)[c]		
			Week 2-3 (suckling)	SC	15 µg	1x	42-43 weeks	12/23 (52%)[c]	16/22 (73%)[c]		
				SC	30 µg (60 µg total)	2x	42-43 weeks	14/14 (100%)[c]	24/24 (100%)[c]		
			Adult[xiii]	SC	15 µg	1x	48-49 weeks	6/12 (50%)[c]	15/33 (45%)[c]		
				SC	30 µg (60 µg total)	2x	48-49 weeks	9/10 (90%)[c]	21/23 (91%)[c]		
				SC	30 µg (180 µg total)	6x	48-49 weeks	12/12 (100%)[c]	13/13 (100%)[c]		

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a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

[xi] Study also included mammary fibroadenomas and fibromas, as well as other types of cancers.
[xii] Includes survivors up to 40 weeks only.
[xiii] 8-9 weeks old.

Chemical	Species, Strain	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors M	Tumors F	Comments	Reference
DMBA Dimethyl-benz(a)anthracene	Mice (Swiss)	Lymphoma	Control	Control	None	N/A	31-52 weeks	3/408 (0.7%)		Higher tumor rates at younger age of exposure. Only one treatment group was exposed IP; others were exposed by subcutaneous injection.	Pietra et al., 1961
			Day 1	IP	30-40 µg	1x	13-33 weeks	6/31 (19%)[c]			
			Day 1	SC	30-40 µg	1x	12-27 weeks	8/27 (30%)[c]			
			Week 8	SC	900 µg	1x	30 weeks	1/13 (8%)[c]			
	Mice (Swiss)	Lung	Control	Control	None	N/A	31-52 weeks	4/408 (0.9%)			
			Day 1	IP	30-40 µg	1x	13-33 weeks	24/31 (77%)[c]			
			Day 1	SC	30-40 µg	1x	12-27 weeks	23/27 (85%)[c]			
			Week 8	SC	900 µg	1x	30 weeks	2/13 (15%)[c]			
DMN Dimethyl-nitrosamine	Rats (Wistar)	Kidney carcinoma	Day 1	IP	20 mg/kg	1x	≥ 5 months	1/33 (3)[c]		In the neonatal group, the dose was reduced to 20 mg/kg in order to achieve approximately equivalent numbers of survivors. No control group.	Hard, 1979
			Day 21		30 mg/kg	1x		5/39 (13)[c]			
			Month 1		30 mg/kg	1x		2/33 (6)[c]			
			Month 1.5		30 mg/kg	1x		1/28 (4)[c]			
			Month 2		30 mg/kg	1x		1/26 (4)[c]			
			Month 3		30 mg/kg	1x		10/27 (37)[c]			
			Month 4		30 mg/kg	1x		7/32 (22)[c]			
			Month 5		30 mg/kg	1x		0/14 (0)[c]			
	Rats (Wistar)	Kidney adenoma	Day 1	IP	20 mg/kg	1x	≥ 5 months	1/33 (3)[c]			
			Day 21		30 mg/kg	1x		13/39 (33)[c]			
			Month 1		30 mg/kg	1x		11/33 (33)[c]			
			Month 1.5		30 mg/kg	1x		13/28 (48)[c]			
			Month 2		30 mg/kg	1x		11/26 (42)[c]			
			Month 3		30 mg/kg	1x		18/27 (67)[c]			
			Month 4		30 mg/kg	1x		17/32 (53)[c]			
			Month 5		30 mg/kg	1x		6/14 (43)[c]			
	Rats (Wistar)	Kidney mesenchymal tumors	Day 1	IP	20 mg/kg	1x	≥ 5 months	8/33 (24)[c]		Mesenchymal tumors were most frequent in the 3 youngest age groups (z test, $p < 0.001$).	
			Day 21		30 mg/kg	1x		18/39 (46)[c]			
			Month 1		30 mg/kg	1x		23/33 (70)[c]			
			Month 1.5		30 mg/kg	1x		5/28 (19)[c]			
			Month 2		30 mg/kg	1x		2/26 (8)[c]			
			Month 3		30 mg/kg	1x		3/27 (11)[c]			
			Month 4		30 mg/kg	1x		7/32 (22)[c]			
			Month 5		30 mg/kg	1x		0/14 (0)[c]			

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a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

Chemical	Species, Strain	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors M	Tumors F	Comments	Reference
DMN Dimethyl-nitrosamine	Rats (Wistar)	Kidney cortical epithelial tumors	Day 1	IP	20 mg/kg	1x	≥ 5 months	2/33 (6)[c]			Hard, 1979
			Day 21		30 mg/kg	1x		16/39 (41)[c]			
			Month 1		30 mg/kg	1x		12/33 (36)[c]			
			Month 1.5		30 mg/kg	1x		14/28 (52)[c]			
			Month 2		30 mg/kg	1x		11/26 (42)[c]			
			Month 3		30 mg/kg	1x		18/27 (67)[c]			
			Month 4		30 mg/kg	1x		21/32 (66)[c]			
			Month 5		30 mg/kg	1x		6/14 (43)[c]			
	Rats (Wistar)	Total tumors	Day 1	IP	20 mg/kg	1x	≥ 5 months	11/33 (33)[c]			
			Day 21		30 mg/kg	1x		25/39 (64)[c]			
			Month 1		30 mg/kg	1x		25/33 (76)[c]			
			Month 1.5		30 mg/kg	1x		17/28 (63)[c]			
			Month 2		30 mg/kg	1x		13/26 (50)[c]			
			Month 3		30 mg/kg	1x		18/27 (67)[c]			
			Month 4		30 mg/kg	1x		22/32 (69)[c]			
			Month 5		30 mg/kg	1x		7/14 (50)[c]			
ENU Ethylnitrosourea	Rats	Nervous system	Day 1	Injection	20 mg/kg	1x		100%[c]		Susceptibility to neuro-oncogenic effect declined with increasing age.	Maekawa and Mitsumori, 1990
			Day 30	Injection	20 mg/kg	1x		61%[c]			
	Mice ($B6C3F_1$)	Liver	Control	Control	None	N/A	90 weeks	1/98 (1%)	0/96 (0%)	Both male and female mice were responsive to exposure during prenatal and infant life.	Vesselinovitch, 1983
			Gestation day 18	IP	60 µg/g body weight	1x		28/52 (54%)[c]	18/49 (37%)[c]		
			Day 15		60 µg/g body weight	1x		41/50 (82%)[c]	28/51 (55%)[c]		
			Day 42		60 µg/g body weight	1x		10/50 (20%)[c]	5/50 (10%)[c]		

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Chemical	Species, Strain	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors		Comments	Reference
								M	F		
	Rats (Wistar)	Nerve tissue	Control	Control	None	N/A	4-7 months	0/16 (0%)	0/10 (0%)	Highest tumor rate seen when exposed during gestation or soon after birth. Statistically significant decrease in tumor incidence with increasing age of exposure.	Naito et al., 1981
			Gestation day 16	IP	40 mg/kg	1x		26/26 (100%)[c]	18/18 (100 %)[c]		
			Day 1	SC	40 mg/kg	1x		12/12 (100%)[a]	16/16 (100 %)[a]		
			Week 1		40 mg/kg	1x		12/17 (71%)[c]	18/20 (90%)[c]		
			Week 2		40 mg/kg	1x		10/14 (71%)[c]	14/18 (78%)[c]		
			Week 3		40 mg/kg	1x		6/13 (46%)[c]	5/17 (29%)[c]		
			Week 4		40 mg/kg	1x		8/15 (53%)[c]	2/10 (20%)[c]		

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a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

Chemical	Species, Strain	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors M	Tumors F	Comments	Reference
ENU Ethylnitrosourea	Mice ($B6C3F_1$)	Lung	Day 1	IP	60 µg/g body weight	1x		49/55 (89%)[c]	49/50 (98%)[c]		Vesselinovitch et al., 1974
			Day 15			1x		50/55 (91%)[c]	47/55 (85%)[c]		
			Day 42			1x		53/59 (90%)[c]	44/51 (86%)[c]		
			Day 1		120 µg/g body weight	1x		36/38 (95%)[c]	54/60 (90%)[c]		
			Day 15			1x		45/49 (92%)[c]	43/50 (86%)[c]		
			Day 42			1x		52/54 (96%)[c]	50/57 (88%)[c]		
	Mice (C3AF1)	Lung	Day 1		60 µg/g body weight	1x		46/47 (98%)[a]	51/51 (100%)[a]		
			Day 15			1x		49/49 (100%)[a]	57/59 (97%)[a]		
			Day 42			1x		59/59 (100%)[a]	57/57 (100%)[a]		
			Day 1		120 µg/g body weight	1x		63/64 (98%)[a]	53/57 (93%)[a]		
			Day 15			1x		54/56 (96%)[a]	50/56 (89%)[a]		
			Day 42			1x		59/59 (100%)[a]	48/48 (100%)[a]		
	Mice ($B6C3F_1$)	Liver	Day 1	IP	60 µg/g body weight	1x		50/54 (93%)[a]	28/43 (65%)[a]		
			Day 15			1x		55/56 (98%)[a]	33/54 (61%)[a]		
			Day 42			1x		12/40 (30%)[c]	6/39 (15%)[c]		
			Day 1		120 µg/g body weight	1x		29/34 (85%)[a]	32/53 (60%)[a]		
			Day 15			1x		45/48 (94%)[a]	29/43 (67%)[a]		
			Day 42			1x		17/49 (35%)[a]	4/50 (8%)[a]		

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Chemical	Species, Strain	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors M	Tumors F	Comments	Reference
	Mice ($C3AF_1$)	Liver	Day 1	IP	60 µg/g body	1x		42/45 (93%)[a]	19/41 (46%)[a]		
			Day 15		weight	1x		42/50 (84%)[a]	19/48 (40%)[a]		
			Day 42			1x		7/29 (24%)[c]	4/50 (8%)[c]		
			Day 1		120 µg/g body	1x		55/62 (89%)[a]	19/45 (42%)[a]		
			Day 15		weight	1x		35/45 (78%)[a]	15/35 (43%)[a]		
			Day 42			1x		8/33 (24%)[c]	3/33 (9%)[c]		
	Mice ($B6C3F_1$)	Kidney	Day 1	IP	60 µg/g body	1x		11/48 (23%)[c]	5/49 (10%)[c]		
			Day 15		weight	1x		6/41 (15%)[c]	7/31 (23%)[c]		
			Day 42			1x		4/40 (10%)[c]	3/37 (8%)[c]		
			Day 1		120 µg/g body	1x		10/30 (33%)[a]	14/53 (26%)[c]		
			Day 15		weight	1x		17/37 (46%)[a]	19/49 (39%)[c]		
			Day 42			1x		8/40 (20%)[c]	11/39 (28%)[c]		
	Mice (C3AF1)	Kidney	Day 1	IP	60 µg/g body	1x		7/44 (16%)[c]	6/45 (13%)[c]		
			Day 15		weight	1x		7/41 (17%)[c]	8/46 (17%)[c]		
			Day 42			1x		3/42 (42%)[c]	3/43 (7%)[c]		
			Day 1		120 µg/g body	1x		4/52 (7%)[c]	6/29 (21%)[a]		
			Day 15		weight	1x		8/35 (23%)[c]	12/29 (41%)[a]		
			Day 42			1x		6/41 (71%)[c]	3/39 (8%)[c]		

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Chemical	Species, Strain	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors M	Tumors F	Comments	Reference
	Mice (B6C3F1)	Haderian	Day 1		60 µg/g body weight	1x		7/40 (17%)[c]	5/43 (12%)[c]		
			Day 15			1x		10/51 (20%)[c]	17/59 (29%)[c]		
			Day 42			1x		14/50 (28%)[c]	14/45 (31%)[c]		
			Day 1		120 µg/g body weight	1x		9/30 (30%)[a]	6/52 (12%)[c]		
			Day 15			1x		15/41 (37%)[a]	8/31 (26%)[c]		
			Day 42			1x		25/48 (52%)[a]	14/49 (29%)[c]		
	Mice (C3AF1)	Haderian	Day 1		60 µg/g body weight	1x		3/25 (12%)[c]	4/35 (11%)[c]		
			Day 15			1x		1/9 (11%)[c]	6/38 (16%)[c]		
			Day 42			1x		12/48 (25%)[c]	5/33 (15%)[c]		
			Day 1		120 µg/g body weight	1x		3/52 (6%)[c]	1/25 (4%)[c]		
			Day 15			1x		6/46 (13%)[c]	2/52 (4%)[c]		
			Day 42			1x		5/29 (17%)[c]	2/11 (18%)[c]		
	Mice (B6C3F1)	Stomach	Day 1		60 µg/g body weight	1x		3/48 (6%)[c]	4/43 (9%)[c]		
			Day 15			1x		10/42 (24%)[a]	7/45 (16%)[c]		
			Day 42			1x		9/51 (18%)[a]	8/36 (22%)[c]		
			Day 1		120 µg/g body weight	1x		2/29 (7%)[c]	9/53 (17%)[c]		
			Day 15			1x		10/35 (29%)[a]	12/33 (36%)[c]		
			Day 42			1x		12/53 (23%)[a]	12/50 (24%)[c]		

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Chemical	Species, Strain	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors		Comments	Reference
								M	F		
	Mice (C3AF1)	Stomach	Day 1		60 µg/g body weight	1x		2/39 (5%)[c]	7/45 (16%)[c]		
			Day 15			1x		7/45 (16%)[a]	7/38 (18%)[c]		
			Day 42			1x		14/55 (25%)[a]	7/49 (14%)[c]		
			Day 1		120 µg/g body weight	1x		8/60 (13%)[c]	9/44 (20%)[c]		
			Day 15			1x		16/51 (31%)[a]	11/42 (26%)[c]		
			Day 42			1x		19/48 (40%)[a]	13/37 (35%)[c]		
	Mice (B6C3F1)	Malignant Lymphomas	Day 1		60 µg/g body weight	1x		2/55 (4%)[c]	6/52 (12%)[a]		
			Day 15			1x		3/56 (5%)[c]	14/59 (24%)[a]		
			Day 42			1x		9/59 (15%)[c]	17/59 (29%)[a]		
			Day 1		120 µg/g body weight	1x		8/39 (20%)[c]	15/65 (23%)[a]		
			Day 15			1x		14/60 (23%)[c]	17/58 (29%)[a]		
			Day 42			1x		12/59 (20%)[c]	14/60 (23%)[a]		
	Mice (C3AF1)	Malignant Lymphomas	Day 1		60 µg/g body weight	1x		6/49 (12%)[c]	8/49 (16%)[a]		
			Day 15			1x		3/49 (6%)[c]	13/61 (21%)[a]		
			Day 42			1x		6/60 (10%)[c]	9/55 (16%)[a]		
			Day 1		120 µg/g body weight	1x		3/66 (5%)[c]	10/58 (17%)[a]		
			Day 15			1x		10/56 (18%)[c]	18/60 (30%)[a]		
			Day 42			1x		3/49 (6%)[c]	13/50 (26%)[a]		

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Chemical	Species, Strain	Target Site	Age when first dosed	Dose Route, # doses	Dose	Duration of exposure	Age at death	Tumor Incidence M	Tumor Incidence F	Comments	Reference
NMU N-nitroso-methylurea	Mice (BC3F1)	Total tumors	Control	Control	N/A	N/A	60 weeks	1/20 (5%)	0%	Control mice did not exhibit tumors in target sites except a single hepatoma in a male control mouse	Terracini and Testa, 1970
		Lung	Day 1	IP	50 µg/g body weight	1x	60 weeks	12/15 (80%)[c]	16/19 (84%)[c]		
			5 weeks		50 µg/g body weight	1x	60 weeks	10/26 (39%)[c]	10/35 (29%)[c]		
		Lympho-sarcoma	Day 1		50 µg/g body weight	1x	60 weeks	23/39 (59%)[c]	23/45 (51%)[c]		
			5 weeks		50 µg/g body weight	1x	60 weeks	11/35 (31%)[c]	21/45 (47%)[c]		
		Liver	Day 1		50 µg/g body weight	1x	60 weeks	10/12 (83%)[c]	1/17 (6%)[c]		
			5 weeks		50 µg/g body weight	1x	60 weeks	0%[c]	0%[b]		
		Kidney	Day 1		50 µg/g body weight	1x	60 weeks	3/15 (20%)[c]	3/18 (17%)[c]		
			5 weeks		50 µg/g body weight	1x	60 weeks	2/21 (10%)[c]	0%[b]		
		Fore-stomach	Day 1		50 µg/g body weight	1x	60 weeks	0%[c]	4/17 (24%)[c]		
			5 weeks		50 µg/g body weight	1x	60 weeks	8/22 (36%)[c]	12/18 (67%)[c]		

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Chemical	Species, Strain	Target Site	Age when first dosed	Dose Route, # doses	Dose	Duration of exposure	Age at death	Tumor Incidence M	Tumor Incidence F	Comments	Reference
NMU N-nitroso-methylurea	Rats (Wistar)	Mammary	Day 1	IP	50 µg/g body weight	1x	60 weeks	0%[c]	4/14 (29%)[c]	Tumor incidence for control rats was based on previous experiments (Della Porta et al., 1968) and was not specifically reported in this paper	Terracini and Testa, 1970
			5 weeks		50 µg/g body weight	1x	60 weeks	0%[c]	3/5 (60%)[c]		
		Lympho-sarcoma	Day 1		50 µg/g body weight	1x	60 weeks	1/10 (10%)[c]	0%[c]		
			5 weeks		50 µg/g body weight	1x	60 weeks	2/8 (25%)[c]	1/11 (9%)[c]		
		Kidney (Ana-plastic)	Day 1		50 µg/g body weight	1x	60 weeks	14/18 (78%)[c]	9/13 (69%)[c]		
			5 weeks		50 µg/g body weight	1x	60 weeks	2/5 (40%)[c]	5/12 (42%)[c]		
		Kidney (Adenoma)	Day 1		50 µg/g body weight	1x	60 weeks	3/14 (21%)[c]	2/6 (33%)[c]		
			5 weeks		50 µg/g body weight	1x	60 weeks	1/4 (25%)[c]	0%[c]		
		Fore-stomach	Day 1		50 µg/g body weight	1x	60 weeks	4/14 (29%)[c]	3/6 (50%)[c]		
			5 weeks		50 µg/g body weight	1x	60 weeks	0%[c]	0%[c]		
		Intestine	Day 1		50 µg/g body weight	1x	60 weeks	3/10 (30%)[c]	2/2 (100%)[c]		
			5 weeks		50 µg/g body weight	1x	60 weeks	2/4 (50%)[c]	0%[c]		

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Chemical	Species, Strain	Target Site	Age when first dosed	Dose Route, # doses	Dose	Duration of exposure	Age at death*	Tumor Incidence		Comments	Reference
								M	F		
NMU N-nitroso-methylurea	Mice (C3Hf/Dp)	Thymus	control	IP	NA	NA	120 wks**	0/34 (0%)	0/25 (0%)	*Age at death from thymic lymphoma reported specifically for some, but not all, dose groups. **Control mice were sacrificed at 120 wks ***Age of death for all mice in this dose group, regardless of cancer type	Terracini et al., 1976
			Day 1		25 µg NMU/g bodyweight	1x	29 ± 8.4 wks	2/16 (13%)[c]	5/25 (20%)[c]		
			Day 70		25 µg NMU/g bodyweight	1x	120 wks (M)*** 100 wks (F)	0/20 (0%)[b]	1/20 (5%)[c]		
			Day 1		50 µg NMU/g bodyweight	1x	16.5 ± 0.7 wks	16/24 (67%)[c]	30/44 (68%)[c]		
			Day 21		50 µg NMU/g bodyweight	1x	24.5 ± 2.5 wks	14/44 (32%)[c]	18/38 (47%)[c]		
			Day 70		50 µg NMU/g bodyweight	1x	31.4 ± 4.4 wks	9/30 (30%)[c]	6/41 (15%)[c]		

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Chemical	Species, Strain	Target Site	Age when first dosed	Dose Route, # doses	Dose	Duration of exposure	Age at death		Tumor Incidence		Reference
							M	F	M	F	
NMU N-nitroso-methylurea	Mice (C3Hf/Dp)	Extra-thymic lymphoma	control	IP	NA	NA	120 weeks	120 weeks	1/34 (3%)	2/25 (8%)	Terracini et al., 1976
			Day 1		25 µg NMU/g bodyweight	1x	100 weeks	90 weeks	2/16 (13%)[c]	1/25 (4%)[c]	
			Day 70		25 µg NMU/g bodyweight	1x	120 weeks	100 weeks	0/20 (0%)[c]	0/20 (0%)[c]	
			Day 1		50 µg NMU/g bodyweight	1x	70 weeks	80 weeks	0/24 (0%)[c]	0/44 (0%)[c]	
			Day 21		50 µg NMU/g bodyweight	1x	100 weeks	90 weeks	1/44 (2%)[c]	0/38 (0%)[c]	
			Day 70		50 µg NMU/g bodyweight	1x	110 weeks	90 weeks	1/30 (3%)[c]	0/41 (0%)[c]	
		Lung	control	IP	NA	NA	120 weeks	120 weeks	4/34 (12%)	6/25 (24%)	
			Day 1		25 µg NMU/g bodyweight	1x	100 weeks	90 weeks	7/16 (44%)[c]	13/25 (52%)[c]	
			Day 70		25 µg NMU/g bodyweight	1x	120 weeks	100 weeks	12/20 (60%)[c]	8/20 (40%)[c]	
			Day 1		50 µg NMU/g bodyweight	1x	70 weeks	80 weeks	5/24 (21%)[c]	11/44 (25%)[c]	
			Day 21		50 µg NMU/g bodyweight	1x	100 weeks	90 weeks	23/44 (52%)[c]	15/38 (39%)[c]	
			Day 70		50 µg NMU/g bodyweight	1x	110 weeks	90 weeks	18/30 (60%)[c]	24/41 (59%)[c]	

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Chemical	Species, Strain	Target Site	Age when first dosed	Dose Route, # doses	Dose	Duration of exposure	Age at death		Tumor Incidence		Reference
							M	F	M	F	
NMU N-nitroso-methylurea	Mice (C3Hf/Dp)	Liver	control	IP	NA	NA	120 weeks	120 weeks	13/34 (38%)	1/25 (4%)	Terracini et al., 1976
			Day 1		25 µg NMU/g bodyweight	1x	100 weeks	90 weeks	9/16 (56%)[a]	2/25 (8%)[c]	
			Day 70		25 µg NMU/g bodyweight	1x	120 weeks	100 weeks	12/20 (60%)[a]	2/20 (10%)[c]	
			Day 1		50 µg NMU/g bodyweight	1x	70 weeks	80 weeks	4/24 (17%)[a]	3/44 (7%)[c]	
			Day 21		50 µg NMU/g bodyweight	1x	100 weeks	90 weeks	21/44 (48%)[a]	1/38 (2.6%)[c]	
			Day 70		50 µg NMU/g bodyweight	1x	110 weeks	90 weeks	8/30 (27%)[a]	2/41 (5%)[c]	
		Stomach	control	IP	NA	NA	120 weeks	120 weeks	0/34 (0%)	5/25 (20%)	
			Day 1		25 µg NMU/g bodyweight	1x	100 weeks	90 weeks	2/16 (13%)[c]	10/25 (40%)[c]	
			Day 70		25 µg NMU/g bodyweight	1x	120 weeks	100 weeks	3/20 (15%)[c]	7/20 (35%)[c]	
			Day 1		50 µg NMU/g bodyweight	1x	70 weeks	80 weeks	2/24 (8%)[c]	1/44 (2%)[c]	
			Day 21		50 µg NMU/g bodyweight	1x	100 weeks	90 weeks	19/44 (43%)[c]	9/38 (24%)[c]	
			Day 70		50 µg NMU/g bodyweight	1x	110 weeks	90 weeks	8/30 (27%)[c]	21/41 (51%)[c]	

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Chemical	Species, Strain	Target Site	Age when first dosed	Dose Route, # doses	Dose	Duration of exposure	Age at death		Tumor Incidence		Reference
							M	F	M	F	
NMU N-nitroso-methylurea	Mice (C3Hf/Dp)	Kidney	control	IP	NA	NA	120 weeks	120 weeks	0/34 (0%)	0/25 (0%)	Terracini et al., 1976
			Day 1		25 µg NMU/g bodyweight	1x	100 weeks	90 weeks	0/16 (0%)[c]	0/25 (0%)[c]	
			Day 70		25 µg NMU/g bodyweight	1x	120 weeks	100 weeks	0/20 (0%)[c]	0/20 (0%)[c]	
			Day 1		50 µg NMU/g bodyweight	1x	70 weeks	80 weeks	0/24 (0%)[c]	4/44 (9%)[c]	
			Day 21		50 µg NMU/g bodyweight	1x	100 weeks	90 weeks	1/44 (2%)[c]	4/38 (11%)[c]	
			Day 70		50 µg NMU/g bodyweight	1x	110 weeks	90 weeks	5/30 (17%)[c]	7/41 (17%)[c]	
		Ovary	control	IP	NA	NA	120 weeks	120 weeks	NA	3/25 (12%)	
			Day 1		25 µg NMU/g bodyweight	1x	100 weeks	90 weeks	NA	2/25 (8%)[c]	
			Day 70		25 µg NMU/g bodyweight	1x	120 weeks	100 weeks	NA	4/20 (20%)[c]	
			Day 1		50 µg NMU/g bodyweight	1x	70 weeks	80 weeks	NA	0/44 (0%)[c]	
			Day 21		50 µg NMU/g bodyweight	1x	100 weeks	90 weeks	NA	9/38 (24%)[c]	
			Day 70		50 µg NMU/g bodyweight	1x	110 weeks	90 weeks	NA	16/41 (39%)[c]	

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Chemical	Species, Strain	Target Site	Age when first dosed	Dose Route, # doses	Dose	Duration of exposure	Age at death		Tumor Incidence		Reference
							M	F	M	F	
NMU N-nitroso-methylurea	Mice (C3Hf/Dp)	Mammary	control	IP	NA	NA	120 weeks	120 weeks	NA	2/25 (8%)	Terracini et al., 1976
			Day 1		25 µg NMU/g bodyweight	1x	100 weeks	90 weeks	NA	1/25 (4%)[c]	
			Day 70		25 µg NMU/g bodyweight	1x	120 weeks	100 weeks	NA	0/20 (0%)[c]	
			Day 1		50 µg NMU/g bodyweight	1x	70 weeks	80 weeks	NA	0/44 (0%)[c]	
			Day 21		50 µg NMU/g bodyweight	1x	100 weeks	90 weeks	1/44 (2%)[c]	0/38 (0%)[c]	
			Day 70		50 µg NMU/g bodyweight		110 weeks	90 weeks	NA	4/41 (9.8%)[c]	
		Uterus or Vagina	control	IP	NA	NA	120 weeks	120 weeks	NA	1/25 (4%)	
			Day 1		25 µg NMU/g bodyweight	1x	100 weeks	90 weeks	NA	1/25 (4%)[c]	
			Day 70		25 µg NMU/g bodyweight	1x	120 weeks	100 weeks	NA	6/20 (30%)[c]	
			Day 1		50 µg NMU/g bodyweight	1x	70 weeks	80 weeks	NA	0/44 (0%)[c]	
			Day 21		50 µg NMU/g bodyweight	1x	100 weeks	90 weeks	NA	1/38 (3%)[c]	
			Day 70		50 µg NMU/g bodyweight		110 weeks	90 weeks		7/41 (17%)[c]	

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a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

Chemical	Species, Strain	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors		Comments	Reference
								M	F		
Urethane	Mice (SWR)	Lung adenoma	Newborn	SC	0.18 mg/g body weight	1x	10 weeks	100%[c]		The average number of tumors per mouse increased linearly with dose.	Kaye and Trainin, 1966
			11-22 weeks	SC	0.25 mg/g body weight	1x	23-34 weeks	0%[c]			
	Mice (C3H/f)	Liver	Control	Control	None	N/A	493 days (m) 553 days (f)	14/97 (14%)	1/77 (1%)		Liebelt et al., 1964
			Day 1	IP	0.8 mg/g body weight	1x	481 days (m) 434 days (f)	27/30 (90%)[a]	18/39 (46%)[a]		
			8-10 weeks	IP	1 mg/g body weight	1x	321 days (m) -	6/25 (24%)[b]	0/32 (0%)[b]		
		Lung	Control	Control	None	N/A	493 days (m) 553 days (f)	0/97 (0%)	0/77 (0%)	The number of lung tumors among the controls was not provided.	
			Day 1	IP	0.8 mg/g body weight	1x	401 days (m) 408 days (f)	14/30 (46%)[a]	19/39 (48%)[a]		
			8-10 weeks	IP	1 mg/g body weight	1x	506 days (m) -	2/25 (8%)[b]	0/32 (0%)[b]		
		Reticular tissue	Control	Control	None	N/A	493 days (m) 553 days (f)	2/97 (2%)	6/77 (8%)		
			Day 1	IP	0.8 mg/g body weight	1x	285 days (m) 343 days (f)	4/30 (13%)[b]	22/39 (56%)[a]		
			8-10 weeks	IP	1 mg/g body weight	1x	- 453 days (f)	0/25 (25%)[b]	4/32 (13%)[b]		
	Mice (Swiss)	Leukemia	Control	Control	None	N/A	8-10 months	1%		Highest tumor rates when dosed at birth. Exposure to newborns was followed by 21.6% leukemia, occurring at a mean age of 105 days.	Fiore-Donati et al., 1962
			Day 1	SC	2 mg in 0.05 ml aqueous solution	1x		13/60 (22%)[c]			
			Day 5		4 mg in 0.05 ml aqueous solution	1x		7/39 (18%)[c]			
			Day 40		20 mg in 0.1 ml aqueous solution	1x		2/63 (3%)[c]			

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a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

Chemical	Species, Strain	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors M	Tumors F	Comments	Reference
Urethane	Mice (Swiss)	Lung adenoma	Control 2 weeks	Control	None	N/A	9 weeks	0/15 (0%)	-	The proportion of animals with adenomas decreased steadily with age of exposure.	Rogers, 1951
			Control 4 weeks	Control	None	N/A	11 weeks	0/14 (0%)	-		
			Control 6 weeks	Control	None	N/A	13 weeks	1/15 (7%)	-		
			Control 8 weeks	Control	None	N/A	15 weeks	2/15 (13%)	-		
			Control 10 weeks	Control	None	N/A	17 weeks	0/15 (0%)	-		
			2 weeks	IP	1 mg/g body weight	1x	9 weeks	24/24 (100%)[c]	-		
			4 weeks	IP	1 mg/g body weight	1x	11 weeks	23/25 (92%)[c]	-		
			6 weeks	IP	1 mg/g body weight	1x	13 weeks	22/25 (88%)[c]	-		
			8 weeks	IP	1 mg/g body weight	1x	15 weeks	21/25 (84%)[c]	-		
			10 weeks	IP	1 mg/g body weight	1x	17 weeks	19/25 (76%)[c]	-		
	Mice (Swiss)	Lung adenoma	3 weeks	IP	0.25 mg/g body weight	1x	12 weeks	16/19 (84%)[c]	-		
					0.5 mg/g body weight	1x	12 weeks	16/20 (80%)[c]	-		
					1 mg/g body weight	1x	12 weeks	18/20 (90%)[c]	-		
			8 weeks	IP	0.25 mg/g body weight	1x	17 weeks	4/17 (24%)[c]	-		
					0.5 mg/g body weight	1x	17 weeks	15/16 (94%)[c]	-		
					1 mg/g body weight	1x	17 weeks	18/18 (100%)[c]	-		

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a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

Chemical	Species, Strain	Target Site	Age when first dosed	Dose Route, # doses	Dose	Duration of exposure	Age at death	Tumor Incidence		Comments	Reference
								M	F		
Urethane	Mice (Swiss)	liver	Control	Control	N/A	N/A	360-720 days	10/227 (4.4%)	4/222 (8.22%)		Chieco-Bianchi et al., 1963
			Day 1	SC	1 mg/g body weight	1x	180 days	1/20 (5%)[a]	0/20 (0%)[b]		
			Day 1	SC	1 mg/g body weight	1x	240 days	2/17 (12%)[a]	0/12 (0%)[b]		
			Day 1	SC	1 mg/g body weight	1x	300 days	5/18 (28%)[a]	0/16 (0%)[b]		
			Day 1	SC	1 mg/g body weight	1x	360 days	11/20 (55%)[a]	0/23 (0%)[b]		
			Day 1	SC	1 mg/g body weight	1x	420 days	13/15 (87%)[a]	2/22 (9%)[a]		
			Day 1	SC	1 mg/g body weight	1x	480 days	17/23 (74%)[b]	2/25 (8%)[b]		
			Day 5	SC	1 mg/g body weight	1x	420 days	9/13 (69.2%)[c]	2/11 (18.2%)[c]		
			Day 20	SC	1 mg/g body weight	1x	420 days	1/13 (8%)[c]	0/16 (0%)[c]		
			Day 40	SC	1 mg/g body weight	1x	420 days	0/11 (0%)[c]	0/9 (0%)[c]		
Urethane	Mice (Swiss)	skin	Control	Control	N/A	N/A	180-550 days	30/712 (4.21%)		Croton oil treatment initiated at 40 days of age	Chieco-Bianchi et al., 1963
			Day 1	SC	1 mg urethane/g body weight; 5% croton oil	single dose urethane, croton oil applied 2x/week for 10 mos	660 days	26/59 (44.1%)[a]			
			Day 40	SC	1 mg urethane/g body weight; 5% croton oil	single dose urethane, croton oil applied 2x/week for 10 mos	700 days	8/41 (19.5%)[c]			

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a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

Chemical	Species, Strain	Target Site	Age when first dosed	Dose Route, # doses	Dose	Duration of exposure	Age at death	Tumor Incidence		Comments	Reference
								M	F		
Urethane	Mice (B6AF1/J)	Liver	Control	gavage	N/A	N/A	71 weeks	1/25 (4%)	0/25 (0%)		Klein, 1966
			Day 1		1 mg/g body weight	1x	66 weeks	9/20 (45%)[a]	9/26 (35%)[a]		
			Day 7		1 mg/g body weight	1x	67 weeks	20/22 (91%)[a]	20/26 (77%)[a]		
			Day 14		1 mg/g body weight	1x	68 weeks	16/20 (80%)[a]	10/23 (43%)[a]		
			Day 21		1 mg/g body weight	1x	69 weeks	13/23 (57%)[a]	1/20 (5%)[a]		
			Day 28		1 mg/g body weight	1x	70 weeks	4/24 (17%)[a]	1/20 (5%)[a]		
		Lung	Control	gavage	1 mg/g body weight	1x	71 weeks	9/25 (36%)	6/25 (24%)		
			Day 1		1 mg/g body weight	1x	66 weeks	20/20 (100%)[c]	25/26 (96%)[c]		
			Day 7		1 mg/g body weight	1x	67 weeks	22/22 (100%)[c]	26/26 (100%)[c]		
			Day 14		1 mg/g body weight	1x	68 weeks	19/20 (95%)[c]	19/23 (83%)[c]		
			Day 21		1 mg/g body weight	1x	69 weeks	23/23 (100%)[c]	19/20 (95%)[c]		
			Day 28		1 mg/g body weight	1x	70 weeks	24/24 (100%)[c]	20/20 (100%)[c]		

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a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

Chemical	Species, Strain	Target Site	Age when first dosed	Dose Route, # doses	Dose	Duration of exposure	Age at death	Tumor Incidence		Comments	Reference
								M	F		
Urethane	Mice (B6AF1/J)	Harderian gland	Control	gavage	1 mg/g body weight	1x	71 weeks	0/25 (0%)	0/25 (0%)		Klein, 1966
			Day 1		1 mg/g body weight	1x	66 weeks	0/20 (0%)[b]	1/26 (4%)[c]		
			Day 7		1 mg/g body weight	1x	67 weeks	0/22 (0%)[b]	1/26 (4%)[c]		
			Day 14		1 mg/g body weight	1x	68 weeks	0/20 (0%)[b]	2/23 (9%)[c]		
			Day 21		1 mg/g body weight	1x	69 weeks	1/23 (4%)[c]	0/20 (0%)[b]		
			Day 28		1 mg/g body weight	1x	70 weeks	0/24 (0%)[b]	0/20 (0%)[b]		
		Fore-stomach	Control	gavage	1 mg/g body weight	1x	71 weeks	0/25 (0%)	1/25 (4%)		
			Day 1		1 mg/g body weight	1x	66 weeks	0/20 (0%)[b]	3/26 (12%)[c]		
			Day 7		1 mg/g body weight	1x	67 weeks	1/22 (5%)[c]	1/26 (4%)[c]		
			Day 14		1 mg/g body weight	1x	68 weeks	1/20 (5%)[c]	4/23 (17%)[c]		
			Day 21		1 mg/g body weight	1x	69 weeks	0/23 (0%)[b]	1/20 (5%)[c]		
			Day 28		1 mg/g body weight	1x	70 weeks	2/24 (8%)[c]	1/20 (5%)[c]		

a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

Supplementary Table S4. Ratio of early-life to adult cancer potencies for studies with repeat exposures of juvenile and adult animals to mutagenic chemicals.

Compound	Species, strain	Sex	Dose	Tumor	Geometric Mean	2.5%	Median	97.5%	Refs.
Benzidine	Mice	male		liver	111	64	**110**	198	Vesselinovitch et al., 1975b
	(B6C3F1)	female		liver	0.16	0.004	**0.22**	1.1	
3 - Methylcholanthrene	Mice	male	0.25 mg/g	hepatoma	33	7.4	**30**	268	Klein, 1959
(formerly known as	(Albino)	female	0.25 mg/g	hepatoma	7.7	1.1	**7.1**	85	
20- Methylcholanthrene)		male	0.25 mg/g	forestomach	0.91	0.39	**0.91**	2.1	
		female	0.25 mg/g	forestomach	1.5	0.58	**1.5**	4.2	
		male	0.25 mg/g	skin	1.8	0.048	**2.1**	22	
		female	0.25 mg/g	skin	1.5	0.023	**1.8**	21	
Safrole	Mice	male		liver	46	16	**44**	198	Vesselinovitch et al., 1979b
	(B6C3F1)	female		liver	0.12	0.002	**0.18**	1.1	
Vinyl Chloride	Rats (Sprague-	male	6000 ppm	liver -angiosarcoma	6.7	0.035	**9.8**	57	Maltoni et al., 1984
	Dawley)	male	10000 ppm	liver -angiosarcoma	7.4	0.035	**11**	62	
		female	6000 ppm	liver -angiosarcoma	13	4.9	**13**	33	
		female	10000 ppm	liver -angiosarcoma	30	8.7	**29**	121	
		male	6000 ppm	zymbal gland	0.73	0.0032	**1.1**	30	
		male	10000 ppm	zymbal gland	0.27	0.0022	**0.4**	5.4	
		female	6000 ppm	zymbal gland	0.48	0.0027	**0.7**	16	
		female	10000 ppm	zymbal gland	0.15	0.0014	**0.19**	4.5	

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Compound	Species, strain	Sex	Dose	Tumor	Geometric Mean	2.5%	Median	97.5%	Refs.
Vinyl Chloride		male	10000 ppm	leukemia	21	0.026	**37**	514	
(cont.)		female	6000 ppm	leukemia	1.3	0.0035	**1.7**	153	
		female	10000 ppm	leukemia	0.29	0.0019	**0.35**	17	
		male	6000 ppm	nephroblastomas	0.15	0.0014	**0.19**	4.8	
		male	10000 ppm	nephroblastomas	0.17	0.0015	**0.21**	6.2	
		female	6000 ppm	nephroblastomas	0.28	0.0018	**0.33**	16	
		female	10000 ppm	nephroblastomas	0.24	0.0017	**0.29**	11	
		male	6000 ppm	angiosarcomas other sites	0.9	0.0033	**1.26**	53	
		male	10000 ppm	angiosarcomas other sites	0.25	0.0017	**0.30**	12	
		female	6000 ppm	angiosarcomas other sites	0.24	0.0017	**0.29**	11	
		female	10000 ppm	angiosarcomas other sites	0.32	0.0019	**0.38**	20	
		male	6000 ppm	angiomas&fibromas other sites	0.72	0.0031	**1.0**	33	
		male	10000 ppm	angiomas&fibromas other sites	1.4	0.0045	**2.36**	47	
		female	6000 ppm	angiomas&fibromas other sites	0.27	0.0018	**0.33**	16	
		female	10000 ppm	angiomas&fibromas other sites	0.52	0.0024	**0.63**	41	
		male	6000 ppm	hepatoma	62	11	**58**	543	
		male	10000 ppm	hepatoma	34	8.2	**32**	218	
		female	6000 ppm	hepatoma	55	13	**51**	352	
		female	10000 ppm	hepatoma	55	8.4	**53**	513	

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Compound	Species, strain	Sex	Dose	Tumor	Geometric Mean	2.5%	Median	97.5%	Refs.
Vinyl Chloride		male	6000 ppm	skin carinomas	1.1	0.0035	**1.5**	82	
(cont.)		male	10000 ppm	skin carinomas	0.41	0.0024	**0.56**	15	
		female	6000 ppm	skin carinomas	0.46	0.0024	**0.59**	24	
		female	10000 ppm	skin carinomas	0.31	0.0019	**0.37**	19	
		male	6000 ppm	neuroblastoma	0.21	0.0016	**0.26**	9.5	
		male	10000 ppm	neuroblastoma	0.20	0.0016	**0.24**	8.5	
		female	6000 ppm	neuroblastoma	0.27	0.0018	**0.32**	15	
		female	10000 ppm	neuroblastoma	0.14	0.0014	**0.18**	4.4	

Supplementary Table S5. Ratio of early-life to adult cancer potencies for studies with lifetime exposures starting with juvenile and adult.

Compound	Species, strain	Sex	Dose	Tumor	Ratio of Juvenile to Adult Potency				Refs.
					Geometric Mean	2.5%	Median	97.5%	
MUTAGENIC COMPOUNDS									
DEN	Rats		multiple	liver	2.8	0.0093	**5.6**	23	(Peto et al. 1984)
	(Colworth)			esophagus	0.18	0.0015	**0.23**	4.8	
Safrole	Mice	male		liver	46	3.7	**50**	253	(Vesselinovitch et al. 1979b)
	(B6C3F1)	female		liver	1.9	0.007	**4.0**	23	
Urethane	Mice	male	2.5 mg/pup	liver	79	0.36	**102**	1064	(Klein 1966)
	(B6AF1/J)	female	2.5 mg/pup	liver	0.47	0.0022	**0.55**	43	
NON-MUTAGENIC COMPOUNDS									
DDT	Mice (B6C3F1)			liver	0.45	0.0023	**0.58**	23	(Vesselinovitch et al. 1979a)
Dieldrin	Mice (B6C3F1)			liver	6.8	0.014	**14**	91	(Vesselinovitch et al. 1979a)
DPH	Rats	male	630:800 ppm	liver	0.31	0.0019	**0.37**	18	(Chhabra et al. 1993b)
	(F344/N)		630:2400 ppm	liver	0.36	0.0021	**0.45**	17	
		female	630:800 ppm	liver	0.33	0.0019	**0.39**	21	
			630:2400 ppm	liver	0.33	0.0019	**0.39**	21	
	Mice	male	210:100 ppm	liver	0.71	0.0028	**0.93**	49	
	($B6C3F_1$)		210:300 ppm	liver	14	0.030	**23**	214	
		female	210:200 ppm	liver	0.32	0.002	**0.42**	13	
			210:600 ppm	liver	0.35	0.0023	**0.53**	8.8	
ETU	Rats	male	90:83 ppm	thyroid	0.23	0.0017	**0.30**	7.3	(Chhabra et al. 1992)
	(F344/N)		90:250 ppm	thyroid	9.1	1.1	**10**	27	

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Compound	Species, strain	Sex	Dose	Tumor	Geometric Mean	2.5%	Median	97.5%	Refs.
ETU (cont.)		female	90:83 ppm	thyroid	0.37	0.0021	**0.46**	19	
			90:250 ppm	thyroid	0.61	0.0034	**1.1**	10	
	Mice ($B6C3F_1$)	male	330:330 ppm	liver	0.37	0.0022	**0.50**	14	
			330:1000 ppm	liver	0.48	0.0027	**0.75**	12	
		female	330:330 ppm	liver	0.33	0.0023	**0.5**	7.8	
			330:1000 ppm	liver	0.42	0.0025	**0.65**	11	
		male	330:330 ppm	thyroid	0.44	0.0022	**0.52**	34	
			330:1000 ppm	thyroid	0.63	0.0035	**1.1**	10	
		female	330:330 ppm	thyroid	5.2	0.011	**10**	108	
			330:1000 ppm	thyroid	0.18	0.0016	**0.24**	4.2	
		male	330:330 ppm	pituitary	0.40	0.0021	**0.47**	32	
			330:1000 ppm	pituitary	0.18	0.0015	**0.22**	5.7	
		female	330:330 ppm	pituitary	0.21	0.0016	**0.26**	10	
			330:1000 ppm	pituitary	0.27	0.0019	**0.36**	9.0	
PBB	Rats (F344/N)	male	10:10 ppm	liver	0.39	0.0023	**0.56**	13	(Chhabra et al. 1993a)
			10:30 ppm	liver	0.18	0.0016	**0.25**	4.3	
		female	10:10 ppm	liver	36	15	**36**	86	
			10:30 ppm	liver	3.1	0.023	**4.6**	22	
		male	10:10 ppm	mononuclear cell leukemia	0.51	0.0025	**0.69**	23	
		male	10:30 ppm	mononuclear cell leukemia	0.77	0.0031	**1.1**	35	
		female	10:10 ppm	mononuclear cell leukemia	0.54	0.0026	**0.74**	24	
		female	10:30 ppm	mononuclear cell leukemia	0.34	0.0021	**0.45**	15	

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Compound	Species, strain	Sex	Dose	Tumor	Geometric Mean	2.5%	Median	97.5%	Refs.
PBB	Mice	male	30:30 ppm	liver	8.9	0.015	**12.2**	1076	
(cont.)	($B6C3F_1$)	female	30:30 ppm	liver	4.4	0.0075	**6.2**	786	
		male	10:10 ppm	liver	0.15	0.0014	**0.20**	3.9	
		female	10:10 ppm	liver	0.29	0.0021	**0.43**	7.0	

Supplementary Table S6. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to mutagenic chemicals.

						Ratio of Juvenile to Adult Potency				
Compound	**Species, strain**	**Sex**	**Dose**	**Tumor**	**Day**	**Geometric Mean**	**2.5%**	**Median**	**97.5%**	**Refs.**
BaP*	Mice (B6C3F1)	male	75 µg/kg	liver	1 day	9.3	2.9	**8.4**	55	Vesselinovitch et al., 1975a
					15 days	11	3.5	**9.6**	61	
		female	75 µg/kg		1 day	1.2	0.0083	**1.6**	31	
					15 days	1.7	0.015	**2.1**	36	
		male	150 µg/kg		1 day	29	8.2	**26**	194	
					15 days	15	4.1	**13**	109	
		female	150 µg/kg		1 day	8.8	1.4	**8.1**	94	
					15 days	1.2	0.0082	**1.6**	30	
	Mice (C3AF1)	male	75 µg/kg	liver	1 day	11	2.1	**10**	112	
					15 days	7.5	1.1	**7.0**	83	
		female	75 µg/kg		1 day	0.2	0.0018	**0.26**	9.1	
					15 days	0.2	0.0017	**0.24**	8.5	
		male	150 µg/kg		1 day	14	3.0	**12.8**	130	
					15 days	3.6	0.11	**3.8**	49	
		female	150 µg/kg		1 day	0.21	0.0017	**0.24**	8.8	
					15 days	0.20	0.0017	**0.24**	8.7	
	Mice (B6C3F1)	male	75 µg/kg	lung	1 day	1.2	0.45	**1.2**	3.4	
					15 days	0.22	0.0046	**0.31**	1.4	
		female	75 µg/kg	lung	1 day	2.8	1.1	**2.7**	9.5	
					15 days	1.4	0.41	**1.4**	5.1	
		male	150 µg/kg	lung	1 day	2.2	1.0	**2.1**	5.4	
					15 days	0.79	0.2	**0.82**	2.3	
		female	150 µg/kg	lung	1 day	7.9	2.6	**7.2**	43	
					15 days	3.7	1.1	**3.4**	22	

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						Ratio of Juvenile to Adult Potency				
Compound	**Species, strain**	**Sex**	**Dose**	Tumor	**Day**	Geometric Mean	**2.5%**	**Median**	**97.5%**	Refs.
BaP* (cont.)	Mice (C3AF1)	male	75 µg/kg	lung	1 day	1.2	0.47	**1.2**	3.2	
					15 days	1.1	0.43	**1.1**	3.1	
		female	75 µg/kg	lung	1 day	1.6	0.66	**1.6**	4.0	
					15 days	1.6	0.71	**1.6**	4.2	
		male	150 µg/kg	lung	1 day	1.5	0.57	**1.5**	5.0	
					15 days	1.9	0.71	**1.8**	6.0	
		female	150 µg/kg	lung	1 day	1.3	0.61	**1.3**	2.9	
					15 days	1.2	0.54	**1.1**	2.6	
DBA	Mice			lung		178	20	**143**	5100	Law, 1940
DEN**	Mice (B6C3F1)	male	6 µg/kg	liver	1 day	9.0	3.5	**8.3**	37	Vesselinovitch et al., 1984
					15 days	8.9	3.5	**8.2**	36	
		female	6 µg/kg	liver	1 day	35	9.1	**31**	239	
					15 days	25	6.3	**226**	175	
		male	12 µg/kg	liver	1 day	9.6	3.3	**8.8**	50	
					15 days	9.8	3.4	**8.9**	51	
		female	12 µg/kg	liver	1 day	16	5.9	**15**	67	
					15 days	19	7.1	**18**	79	
	Mice (C3AF1)	Male	6 µg/kg	liver	1 day	7.3	2.9	**6.9**	26	
					15 days	3.5	1.4	**3.3**	13	
		female	6 µg/kg	liver	1 day	17	3.2	**16**	166	
					15 days	6.4	0.86	**6.0**	73	
		Male	12 µg/kg	liver	1 day	11	3.7	**9.5**	53	
					15 days	9.8	3.4	**8.9**	50	
		female	12 µg/kg	liver	1 day	40	8.5	**36**	340	
					15 days	25	5.0	**22**	221	

Continued, next page

						Ratio of Juvenile to Adult Potency				
Compound	**Species, strain**	**Sex**	**Dose**	Tumor	**Day**	Geometric Mean	**2.5%**	**Median**	**97.5%**	Refs.
DEN** (cont.)	Mice (B6C3F1)	male	6 µg/kg	lung	1 day	0.51	0.27	**0.52**	0.93	Vesselinovitch et al., 1984
					15 days	1.6	0.95	**1.6**	2.7	
		female	6 µg/kg	lung	1 day	0.89	0.54	**0.89**	1.5	
					15 days	1.2	0.76	**1.2**	2.0	
		male	12 µg/kg	lung	1 day	0.40	0.21	**0.40**	0.73	
					15 days	0.66	0.39	**0.66**	1.1	
		female	12 µg/kg	lung	1 day	0.72	0.44	**0.73**	1.2	
					15 days	1.4	0.88	**1.4**	2.3	
	Mice (C3AF1)	male	6 µg/kg	lung	1 day	0.66	0.22	**0.67**	1.7	
					15 days	0.54	0.21	**0.56**	1.3	
		female	6 µg/kg	lung	1 day	1.1	0.45	**1.1**	2.5	
					15 days	0.74	0.36	**0.74**	1.5	
		male	12 µg/kg	lung	1 day	0.31	0.084	**0.33**	0.76	
					15 days	0.61	0.26	**0.62**	1.4	
		female	12 µg/kg	lung	1 day	0.75	0.35	**0.75**	1.6	
					15 days	0.75	0.37	**0.75**	1.5	
DMBA[#]	Rats (Wistar)	male		total	2v5-8 wks	3.3	1.3	**3.2**	10	Meranze et al., 1969
					2v26 wks	3.2	1.3	**3.1**	9.7	
		female		total	2v5-8 wks	1.3	0.68	**1.3**	2.5	
					2v26 wks	3.3	1.2	**3.0**	16	
				mammary	2v5-8 wks	0.041	0.0012	**0.056**	0.26	
					2v26 wks	0.22	0.0023	**0.29**	5.3	
					5v26 wks	7.1	1.8	**6.4**	55	
	Mice (Balb/c)	male	15 µg	lung	1 day	30	2.8	**22**	1482	Walters, 1966
					15-19 days	1.0	0.28	**1.0**	3.5	
		male	30 µgx2	lung	15-19 days	14	1.1	**10**	978	
		female	15 µg	lung	1 day	60	6.0	**46**	2350	
					15-19 days	3.1	0.51	**3.0**	22	
		female	30 µgx2	lung	15-19 days	15	1.2	**11**	1004	
	Mice (Swiss)			lymphoma		2.7	0.60	**2.5**	19	Pietra et al., 1961
				lung		9.1	2.9	**8.7**	40	

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						Ratio of Juvenile to Adult Potency				
Compound	**Species, strain**	**Sex**	**Dose**	**Tumor**	**Day**	Geometric Mean	**2.5%**	**Median**	**97.5%**	**Refs.**
DMN***	Rats (Wistar)		3 wks	total	1 month	0.73	0.41	**0.73**	1.3	Hard, 1979
					1.5 months	1.1	0.58	**1.1**	2.1	
					2 months	1.5	0.75	**1.5**	3.0	
					3 months	0.94	0.50	**0.94**	1.8	
			24 hr		1 month	0.28	0.13	**0.28**	0.6	
					1.5 months	0.42	0.18	**0.42**	0.9	
					2 months	0.56	0.24	**0.56**	1.3	
					3 months	0.36	0.16	**0.36**	0.78	
			1 month		1.5 months	1.5	0.80	**1.5**	3.0	
					2 months	2.0	1.0	**2.0**	4.2	
					3 months	1.3	0.69	**1.3**	2.5	
ENU	Mice (B6C3F1)	male		liver		7.8	3.9	**7.7**	18	Vesselinovitch, 1983
		female				7.1	2.9	**6.9**	21	
	Rats (Wistar)	male		nerve tissue	1 day	27	2.5	**20**	1374	Naito et al., 1981
					1 week	1.6	0.61	**1.6**	4.6	
					2 weeks	1.6	0.58	**1.6**	4.8	
					3 weeks	0.68	0.12	**0.72**	2.3	
		female			1 day	64	6.0	**50**	2488	
					1 weeks	9.6	2.6	**8.9**	59	
					2 weeks	6.2	1.6	**5.7**	40	
					3 weeks	0.69	0.0090	**0.89**	8.9	
	Mice (B6C3F1)	male	60 µg/g	lung	1	1.0	0.60	**1.0**	1.7	Vesselinovitch et al., 1974
					15	1.1	0.66	**1.1**	1.8	
		female	60 µg/g	lung	1	2.1	1.17	**2.1**	4.1	
					15	1.0	0.60	**1.0**	1.7	
		male	120 µg/g	lung	1	1.0	0.60	**1.0**	1.7	
					15	1.1	0.66	**1.0**	1.8	
		female	120 µg/g	lung	1	2.1	1.2	**2.1**	4.1	
					15	1.0	0.60	**1.0**	1.7	

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Compound	Species, strain	Sex	Dose	Tumor	Ratio of Juvenile to Adult Potency					Refs.
					Day	Geometric Mean	2.5%	Median	97.5%	
ENU (cont.)	Mice (C3AF1)	male	60 µg/g	lung	1	8.7	2.7	**8.0**	48	
					15	52	5.2	**39**	2141	
		female	60 µg/g	lung	15	0.71	0.32	**0.72**	1.6	
		male	120 µg/g	lung	1	0.92	0.38	**0.92**	2.2	
					15	0.67	0.28	**0.67**	1.6	
		female	120 µg/g	lung	1	0.54	0.24	**0.54**	1.2	
					15	0.42	0.18	**0.42**	0.92	
	Mice (B6C3F1)	male	60 µg/g	liver	1	8.8	4.2	**8.5**	22	
					15	14	6.2	**14**	37	
		female	60 µg/g	liver	1	6.3	2.6	**6.1**	18	
					15	5.6	2.4	**5.4**	16	
		male	120 µg/g	liver	1	5.2	2.5	**5.1**	11	
					15	7.6	3.9	**7.5**	17	
		female	120 µg/g	liver	1	11	4.1	**11**	46	
					15	14	4.9	**13**	55	
	Mice- (C3AF1)	male	60 µg/g	liver	1	12	4.7	**11**	43	
					15	8.1	3.2	**7.6**	29	
		female	60 µg/g	liver	1	7.5	2.6	**7.0**	32	
					15	4.8	1.8	**4.6**	18	
		male	120 µg/g	liver	1	9.8	4.1	**9.3**	32	
					15	6.6	2.7	**6.3**	23	
		female	120 µg/g	liver	1	5.4	1.7	**5.0**	25	
					15	5.4	1.7	**5.1**	25	
	Mice (B6C3F1)	male	60 µg/g	kidney	1	2.2	0.73	**2.1**	8.0	
					15	1.2	0.29	**1.2**	5.1	
		female	60 µg/g	kidney	1	0.72	0.024	**0.85**	5.9	
					15	2.6	0.61	**2.5**	15	
		male	120 µg/g	kidney	1	1.7	0.65	**1.7**	4.4	
					15	2.6	1.1	**2.6**	6.4	
		female	120 µg/g	kidney	1	0.87	0.37	**0.87**	2.0	
					15	1.4	0.67	**1.4**	3.2	

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Compound	Species, strain	Sex	Dose	Tumor	Day	Ratio of Juvenile to Adult Potency				Refs.
						Geometric Mean	2.5%	Median	97.5%	
ENU (cont.)	Mice (C3AF1)	male	60 µg/g	kidney	1	1.8	0.17	**1.9**	15	
					15	2.0	0.25	**2.0**	16	
		female	60 µg/g	kidney	1	1.0	0.016	**1.3**	13	
					15	2.1	0.16	**2.2**	20	
		male	120 µg/g	kidney	1	0.17	0.0029	**0.24**	1.5	
					15	1.5	0.38	**1.5**	5.9	
		female	120 µg/g	kidney	1	2.3	0.17	**2.4**	20	
					15	7.1	1.8	**6.5**	47	
	Mice (B6C3F1)	male	60 µg/g	Harderian	1	0.34	0.018	**0.41**	1.4	
					15	0.48	0.075	**0.52**	1.4	
		female	60 µg/g	Harderian	1	0.11	0.0025	**0.16**	0.74	
					15	0.84	0.35	**0.84**	2.0	
		male	120 µg/g	Harderian	1	0.41	0.13	**0.42**	0.96	
					15	0.57	0.26	**0.57**	1.2	
		female	120 µg/g	Harderian	1	0.13	0.0030	**0.18**	0.85	
					15	0.72	0.17	**0.77**	2.1	
	Mice (C3AF1)	male	60 µg/g	Harderian	1	0.14	0.0023	**0.20**	1.3	
					15	0.13	0.0016	**0.18**	1.8	
		female	60 µg/g	Harderian	1	0.43	0.019	**0.52**	2.5	
					15	0.81	0.15	**0.85**	3.4	
		male	120 µg/g	Harderian	1	0.065	0.0010	**0.086**	1.0	
					15	0.29	0.0050	**0.40**	2.8	
		female	120 µg/g	Harderian	1	0.074	0.0012	**0.094**	1.2	
					15	0.064	0.0012	**0.081**	0.90	
	Mice (B6C3F1)	male	60 µg/g	Stomach	1	0.28	0.0091	**0.34**	2.4	
					15	1.9	0.61	**1.82**	8.7	
		female	60 µg/g	Stomach	1	0.21	0.0083	**0.26**	1.1	
					15	0.19	0.0072	**0.24**	1.0	
		male	120 µg/g	Stomach	1	0.16	0.0059	**0.20**	0.90	
					15	1.2	0.50	**1.2**	2.9	
		female	120 µg/g	Stomach	1	0.58	0.19	**0.60**	1.5	
					15	1.6	0.67	**1.6**	3.7	

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Compound	Species, strain	Sex	Dose	Tumor	Day	Ratio of Juvenile to Adult Potency				Refs.
						Geometric Mean	2.5%	Median	97.5%	
ENU (cont.)	Mice (C3AF1)	male	60 µg/g	Stomach	1	0.046	0.0009	**0.063**	0.51	
					15	0.35	0.023	**0.41**	1.3	
		female	60 µg/g	Stomach	1	0.81	0.085	**0.89**	3.5	
					15	1.1	0.19	**1.1**	4.5	
		male	120 µg/g	Stomach	1	0.16	0.010	**0.19**	0.56	
					15	0.69	0.32	**0.70**	1.5	
		female	120 µg/g	Stomach	1	0.44	0.14	**0.46**	1.2	
					15	0.63	0.24	**0.64**	1.5	
NMU	Mice (BC3F1)	male	50 µg/g	lung adenomas	1	3.4	1.3	**3.3**	9.3	Terracini and Testa, 1970
		female	50 µg/g	lung adenomas	1	6.3	2.4	**6.0**	23	
		male	50 µg/g	lymphsarcoma	1	2.5	1.1	**2.4**	6.4	
		female	50 µg/g	lymphsarcoma	1	1.1	0.49	**1.1**	2.4	
		male	50 µg/g	hepatoma	1	35	6.5	**32**	324	
		female	50 µg/g	hepatoma	1	0.31	0.0023	**0.39**	13	
		male	50 µg/g	Renal adenoma	1	0.86	0.0093	**1.2**	13	
		female	50 µg/g	Renal adenoma	1	1.3	0.0081	**1.7**	33	
		male	50 µg/g	forestomach	1	0.032	0.0006	**0.039**	0.52	
		female	50 µg/g	forestomach	1	0.11	0.0027	**0.15**	0.69	

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Compound	Species, strain	Sex	Dose	Tumor	Day	Ratio of Juvenile to Adult Potency				Refs.
						Geometric Mean	2.5%	Median	97.5%	
NMU (cont.)	Mice (C3Hf/Dp)	male	25 µg/g	thymic lymphoma	1	1.9	0.048	**2.1**	23	
		female	25 µg/g	thymic lymphoma	1	1.2	0.0089	**1.5**	30	
		male	25 µg/g	lung adenomas	1	0.95	0.013	**1.2**	11	
		female	25 µg/g	lung adenomas	1	0.38	0.018	**0.46**	1. 7	
		male	25 µg/g	liver tumor	1	0.16	0.0016	**0.21**	4.6	
		female	25 µg/g	liver tumor	1	0.26	0.0026	**0.39**	4.4	
		male	25 µg/g	Stomach	1	0.47	0.0045	**0.67**	6.8	
		female	25 µg/g	Stomach	1	0.32	0.0046	**0.43**	3.8	
				ovarian	1	0.13	0.0014	**0.17**	3.5	
				uterine/vaginal	1	8.6	1.1	**8.1**	97	
		male	50 µg/g	thymic lymphoma	1	7.9	3.1	**7.4**	30	
		female	50 µg/g	thymic lymphoma	1	3.1	1.3	**3.0**	7.8	
		male	50 µg/g	lung adenomas	1	0.042	0.0008	**0.058**	0.45	
		female	50 µg/g	lung adenomas	1	0.059	0.0012	**0.084**	0.53	
		male	50 µg/g	liver tumor	1	0.25	0.0021	**0.33**	7.8	
		female	50 µg/g	liver tumor	1	0.11	0.0011	**0.13**	4.5	
		male	50 µg/g	Stomach	1	0.011	0.0003	**0.013**	0.12	
		female	50 µg/g	Stomach	1	0.11	0.0022	**0.15**	0.96	
				ovarian	1	0.011	0.0003	**0.014**	0.14	
				uterine/vaginal	1	0.028	0.0005	**0.034**	0.46	
		male	50 µg/g	thymic lymphoma	21	4.3	1. 6	**4.1**	17	
		female	50 µg/g	thymic lymphoma	21	1.0	0.39	**1.0**	2.6	
		male	50 µg/g	lung adenomas	21	0.14	0.0022	**0.22**	1.1	
		female	50 µg/g	lung adenomas	21	0.74	0.30	**0.75**	1.7	
		male	50 µg/g	liver tumor	21	0.12	0.0013	**0.15**	4.3	
		female	50 µg/g	liver tumor	21	0.92	0.0051	**1.4**	23	
		male	50 µg/g	Stomach	21	0.057	0.001	**0.08**	0.64	
		female	50 µg/g	Stomach	21	1.8	0.77	**1.8**	4.7	
				ovarian	21	0.044	0.0007	**0.055**	0.97	
				uterine/vaginal	21	1.7	0.59	**1.7**	6.4	

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						Ratio of Juvenile to Adult Potency				
Compound	**Species, strain**	**Sex**	**Dose**	**Tumor**	**Day**	**Geometric Mean**	**2.5%**	**Median**	**97.5%**	**Refs.**
Urethane	Mice (Swiss)	male	1 mg/g	liver	1	24	4.4	**21**	220	Chieco-Bianchi et al., 1963
		female	1 mg/g	liver	1	0.44	0.0044	**0.54**	13	
		male	1 mg/g	liver	5	14	2.4	**13**	137	
		female	1 mg/g	liver	5	1.2	0.017	**1.4**	26	
		male	1 mg/g	liver	20	0.23	0.0018	**0.28**	10	
		female	1 mg/g	liver	20	0.10	0.0011	**0.12**	4.8	
		both	1 mg/g	skin	1	0.24	0.0027	**0.32**	5.4	
Urethane + croton oil	Mice (Swiss)	both	1 mg/g	skin	1	2.9	1.2	**2.8**	8.2	
Urethane	Rats (MRC Wistar-derived)	male/ female	16%x6	neurilemmomas	1	0.24	0.0028	**0.33**	4.5	Choudari Kommineni et al., 1970
		male/ female	16%x6	neurilemmomas	28	0.39	0.0045	**0.51**	6.3	
		male/ female	16%x6	liver	1	7.9	1.4	**7.1**	82	
		male/ female	16%x6	liver	28	0.23	0.0026	**0.4**	11.7	
		male/ female	16%x6	thyroid	1	0.032	0.0006	**0.039**	0.67	
		male/ female	16%x6	thyroid	28	0.079	0.0011	**0.1**	1.5	
	Mice (Swiss)	male/ female	1 mg/g	lung	1	15	1.2	**11**	997	De Benedictis et al., 1962
	Mice (Swiss)			leukemia		6.7	1.7	**6.1**	45	Fiore-Donati et al., 1962
						5.1	1.1	**4.7**	38	

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Compound	Species, strain	Sex	Dose	Tumor	Day	Ratio of Juvenile to Adult Potency				Refs.
						Geometric Mean	2.5%	Median	97.5%	
Urethane (cont.)	Mice (B6AF1/J)	male	1 mg/g	liver	21	5.1	1.4	**4.7**	30	Klein, 1966
		female	1 mg/g	liver	21	0.20	0.0019	**0.26**	6.0	
				Harderian gland	1	0.26	0.0021	**0.33**	11	
					7	0.26	0.0021	**0.33**	11	
					14	0.64	0.0044	**0.85**	20	
		male	1 mg/g	Harderian gland	21	0.32	0.0024	**0.41**	13	
		male	1 mg/g	Forestomach	1	0.065	0.0009	**0.079**	1.9	
		female	1 mg/g	Forestomach	1	0.36	0.0028	**0.49**	11	
		male	1 mg/g	Forestomach	7	0.15	0.0017	**0.19**	3.5	
		female	1 mg/g	Forestomach	7	0.13	0.0013	**0.16**	5.0	
		male	1 mg/g	Forestomach	14	0.16	0.0018	**0.21**	3.9	
		female	1 mg/g	Forestomach	14	0.79	0.0056	**1.1**	18	
		male	1 mg/g	Forestomach	21	0.060	0.0008	**0.072**	1.7	
	Mice (B6AF1/J)	female	1 mg/g	Forestomach	21	0.16	0.0015	**0.2**	6.3	
				lung	1	0.95	0.36	**0.95**	2.5	
		male	1 mg/g	lung	14	0.79	0.26	**0.8**	2.3	
		female	1 mg/g	lung	14	0.44	0.16	**0.45**	1.1	
					21	0.86	0.31	**0.86**	2.4	
	Mice (C3H/f)	male	1 mg/g	liver	1	14	4.0	**12**	81	Liebelt et al., 1964
		female	1 mg/g	liver	1	16	3.2	**15**	155	
		male	1 mg/g	lung	1	5.9	1.7	**5.6**	28	
		female	1 mg/g	lung	1	22	4.5	**20**	203	
		male	1 mg/g	reticular tissue	1	2.0	0.023	**2.3**	38	
		female	1 mg/g	reticular tissue	1	8.6	2.3	**7.7**	60	
	Mice (Swiss)		1 mg/g	pulmonary adenomas	2vs4 weeks	14	1.1	**10.1**	965	Rogers, 1951
			1 mg/g	pulmonary adenomas	2vs6 weeks	16	1.3	**11.3**	1025	
			1 mg/g	pulmonary adenomas	2vs8 weeks	19	1.6	**13.3**	1126	
			1 mg/g	pulmonary adenomas	2vs10 weeks	21	1.9	**14.5**	1168	
			0.25 mg/g	adenomas	3vs8week	7.1	2.3	**6.7**	29	
			0.5 mg/g	adenomas	3vs8week	0.67	0.29	**0.67**	1.6	
			1.0 mg/g	adenomas	3vs8week	0.68	0.28	**0.68**	1.6	

Supplementary Table S7. Coefficients for the revised methodology mortality risk model (from U.S. EPA, 1999)

[The coefficients were derived using several models applied to data from A-bomb survivors and selected medical exposures.]

Cancer type	Risk model type[a]	Age Group				
		0-9	10-19	20-29	30-39	40+
Male:						
Stomach	R	1.223	1.972	2.044	0.3024	0.2745
Colon	R	2.290	2.290	0.2787	0.4395	0.08881
Liver	R	0.9877	0.9877	0.9877	0.9877	0.9877
Lung	R	0.4480	0.4480	0.0435	0.1315	0.1680
Bone	A	0.09387	0.09387	0.09387	0.09387	0.09387
Skin	A	0.06597	0.06597	0.06597	0.06597	0.06597
Breast	R	0.0	0.0	0.0	0.0	0.0
Ovary	R	0.0	0.0	0.0	0.0	0.0
Bladder	R	1.037	1.037	1.037	1.037	1.037
Kidney	R	0.2938	0.2938	0.2938	0.2938	0.2938
Thyroid	A	0.1667	0.1667	0.1667	0.1667	0.1667
Leukemia	R	982.3	311.3	416.6	264.4	143.6
Female:						
Stomach	R	3.581	4.585	4.552	0.6309	0.5424
Colon	R	3.265	3.265	0.6183	0.8921	0.1921
Liver	R	0.9877	0.9877	0.9877	0.9877	0.9877
Lung	R	1.359	1.359	0.1620	0.4396	0.6047
Bone	A	0.09387	0.09387	0.09387	0.09387	0.09387
Skin	A	0.06597	0.06597	0.06597	0.06597	0.06597
Breast	R	0.7000	0.7000	0.3000	0.3000	0.1000
Ovary	R	0.7185	0.7185	0.7185	0.7185	0.7185
Bladder	R	1.049	1.049	1.049	1.049	1.049
Kidney	R	0.2938	0.2938	0.2938	0.2938	0.2938

[a] A= absolute risk with coefficient units of 10^{-4} $(Gy\ y)^{-1}$; R= relative risk with coefficient units of Gy^{-1}

Thyroid	A	0.3333	0.3333	0.1667	0.1667	0.1667
Leukemia	R	1176	284.9	370.06	178.8	157.1

Supplementary Table S8. Example of difference in study design sensitivity between lifetime and repeated exposure studies for 10-fold greater risk from juvenile exposure for animals with a 98 week lifespan.

	Number of animals with tumors (n=50)		
	Control	**Early-life Exposure[a]**	**Adult Exposure[b]**
Lifetime	1	36	30
Repeated	1	16	30

[a]. 98 weeks of exposure for lifetime design (4 weeks as juvenile and 94 weeks as adult) and 4 weeks of exposure for repeat design.
[b]. 94 weeks of exposure.

Supplementary Table S9. Excess Relative Risk estimates for cancer incidence from Life Span Study (Japanese survivors)[a] The ERR is the increased cancer rate relative to an unexposed population; an ERR of 1 corresponds to a doubling of the cancer rate.

Site	Average Excess Relative Risk at 1 Sievert	
	Age at Exposure	
	<20	>20
Stomach	0.74	0.24
Colon	0.62	0.7
Liver	1.3	0.31
Lung	0.57	1.1
Bone & connective tissue	11	0.42
Skin	5.4	0.39
Breast	3.3	0.98
Urinary bladder	0.71	0.79
Leukemia	6.1	3.7

[a]. Information based on tables in Annex I of UNSCEAR 2000

Supplementary Table S10. Excess Relative Risk estimates for incidence of thyroid cancer from Life Span Study[i] The ERR is the increased cancer rate relative to an unexposed population; an ERR of 1 corresponds to a doubling of the cancer rate.

Age at exposure	Average Excess Relative Risk at 1 Sievert (No. cases)
0-9 yr	10.25 (24)
10-19 yr	4.5 (35)
20-29 yr	0.10 (18)
>30 yr	0.04 (55)

[i]. Information based on tables in Annex 1 of UNSCEAR 2000.