

Substance	Human	Malformations in Humans	Human Reference Type	Reproductive Toxicity per NTP	Mammal	Rat	Malformations in Rats	Mouse	Malformations in Mice
Acetaminophen; 4-prime.-Hydroxyacetanilide; N-(4-Hydroxyphenyl)acetamide; Paracetamol	-		Case rpts, epi. Studies	m -, f +	-			-	387 mg/kg
Acetone; 2-Propanone; Dimethyl ketone	-	birth defects not specified	Case repts		-	-		-	
2-Acetylaminofluorene; 2-AAF; 2-Acetamidofluorene; N-2-Fluorenylacetamide									
Acrylamide; 2-Propenamide				m +, f -	-	-	15 mg/kg	-	7.5-15 mg/kg
Actinomycin D; Dactinomycin; Cosmegen (Merck & Co.)					+	+	Injection of 25-100 µg/kg before day 10 of pregnancy caused craniorachischisis and other nervous system malformations		
Amaranth; FD&C Red No. 2					-	-		-	
6-Aminonicotinamide; 6-Amino-3-nvridinecarboxamide					+			+	cleft palate-9 mg/kg
Ascorbic acid; L-Ascorbic acid; Vitamin C	-		Epi. study and case-control study		-	-		-	1000 mg/kg
Aspartame; asp-phe methyl ester	-	49-58 mg/kg	Epi. study		-	-	1% in diet	-	1 - 4g/kg
Atrazine					-	-		-	
5-Azacytidine; Azacitidine; 4-Amino-1-.beta.-D-ribofuranosyl-1.3.5-triazin-2(1H)-one					+	+	exencephaly - 1 mg/kg	+	exencephaly - 1 mg/kg
Benzo[a]pyrene				m +, f -	-	-	some resorptions at 1% in diet	-	clubfoot in some mice with Ah receptor - 300 mg/kg
Benzoyl Hydrazine				m +, f -					

Substance	Rabbit	Malformations in Rabbits	Other Animals	Malformations in Other Animals	References
Acetaminophen; 4,prime.-Hydroxyacetanilide; N-(4-Hydroxyphenyl)acetamide; Paracetamol					Shepard 1992; Copp 1990
Acetone; 2-Propanone; Dimethyl ketone	-				Shepard 1992; Schardein 1993
2-Acetylaminofluorene; 2-AAF; 2-Acetamidofluorene; N-2-Fluorenylacetamide					
Acrylamide; 2-Propenamide					Shepard 1992
Actinomycin D; Dactinomycin; Cosmegen (Merck & Co.)	+	agenesis of the optic nerve, encephalocele and lumbosacral spina bifida (120 - 250 ug/day)			Szabo 1989; Shepard 1992
Amaranth; FD&C Red No. 2	-				Smith 1983
6-Aminonicotinamide; 6-Amino-3-nvridinecarboxamide					Diehl 1997
Ascorbic acid; L-Ascorbic acid; Vitamin C					Schardein 1993; Shepard 1992
Aspartame; asp-phe methyl ester					Shepard 1992
Atrazine	-		-	chick embryos	Schardein 1993; Henshel 1996
5-Azacytidine; Azacitidine; 4-Amino-1-.beta.-D-ribofuranosyl-1.3.5-triazin-2(1H)-one					Copp1990; Schardein 1993
Benzo[a]pyrene					Shepard 1992
Benzoyl Hydrazine					

Substance	Human	Malformations in Humans	Human Reference Type	Reproductive Toxicity per NTP	Mammal	Rat	Malformations in Rats	Mouse	Malformations in Mice
Bisphenol A; 4,4'-(1-methylpropylidene) bisphenol; 4,4'-isopropylidenediphenol	-		Epi. study and case reports	m +, f -	-	-	160-1280 mg/kg	-	500-1250 mg/kg
Boric Acid	-				+	+		+	
3-Butyn-1-ol				m +, f -					
3-Butyn-2-ol				m +, f -					
2-Butyne-1,4-diol				m +, f -	-	-	80 mg/kg		
Cadmium chloride	-		Lit. review and case studies	m +, f -	+	+	16 micromoles/kg - eye defects, hydrocephaly	+	
Caffeine	-		Lit. review and case studies	m +, f -	+	+	80-200 mg/kg	+	50-250 mg/kg
Coal-derived fuel oil blend (CRM 1)					+	+	embryoethality; cleft palate, 0.66 mg/L		
Cobalt chloride; Cobaltous chloride					-	-			
Copper (1)					-	-	0.2 mg/m3 - embryoethality		
Copper (2)					-	-			
Copper chloride; Cupric chloride					-	-			
Copper sulfate					+			+	
Cotinine					-	-			
Coumarin	+	hydrocephaly			-			-	0.25% in diet
Cycloheximide					+	+	embryoethality - 1 mg/kg	+	resorptions - 10 mg/kg; polydactyly, oligodactyly - 30 mg/kg
Cyclophosphamide	+	digit and other anomalies			+	+	7-10 mg/kg	+	20 mg/kg
Cytochalasin D					+	-		+	1.1 mg/kg - exencephaly in BALBc mice
Cytosine arabinoside; Cytarabine	+			m -, f +	+	+	20-800 mg/kg - cleft palate	+	20-800 mg/kg - cleft palate
Desisopropyl atrazine				m -, f +	+			+	
Diazepam; Valium; 7-Chloro-1-methyl-5-phenyl-3H-1,4-benzodiazepin-2(1H)-one	+			m -, f +	+	-	200 mg/kg	+	140 mg/kg

Substance	Rabbit	Malformations in Rabbits	Other Animals	Malformations in Other Animals	References
Bisphenol A; 4,4'-(1-methylpropylidene) bisphenol; 4,4'-isopropylidenediphenol					Schwetz 1993
Boric Acid	+			rumpleness (2.5 mg at 24 hours), facial and palate defects appeared after the same dose at day 4	Schardein 1993; Shepard 1992
3-Butyn-1-ol					
3-Butyn-2-ol					
2-Butyne-1,4-diol					Hellwig 1997
Cadmium chloride					Shepard 1992
Caffeine	+	100 mg/kg			Smith 1983
Coal-derived fuel oil blend (CRM 1)					Shepard 1992
Cobalt chloride; Cobaltous chloride					Paternain 1988; Leonard 1990
Copper (1)					Shepard 1992
Copper (2)					Shepard 1992
Copper chloride; Cupric chloride					Shepard 1992
Copper sulfate					Schardein 1993
Cotinine					Baldwin 1988
Coumarin	-	10-100X therapeutic dose			Smith 1983; Schardein 1993
Cycloheximide					Shepard 1992
Cyclophosphamide	+	30 mg/kg	chicks	5-10 mg/kg	Schardein 1993
Cytochalasin D					Copp 1990; Smith 1983; Shepard 1992
Cytosine arabinoside; Cytarabine			- (chicks)	facial and skeletal defects	Shepard 1992
Desisopropyl atrazine					Schardein 1993
Diazepam; Valium; 7-Chloro-1-methyl-5-phenyl-3H-1,4-benzodiazepin-2(1H)-one					Smith 1983; Schardein 1993

Substance	Human	Malformations in Humans	Human Reference Type	Reproductive Toxicity per NTP	Mammal	Rat	Malformations in Rats	Mouse	Malformations in Mice
Dichloroacetate					+	+	cardiovascular defects		
Dichloroacetic acid				m -, f +	+	+	cardiovascular - 400 mg/kg		
2,4-D; 2,4-dichlorophenoxyacetic acid				m -, f +					
Diethylene glycol				m -, f +	-				
Dimethyl sulfoxide; DMSO					-	-	8 g/kg	-	8 g/kg
Diphenhydramine hydrochloride; Benadryl [registered]	-		epi studies		-	-	4-20 mg/kg	-	80 mg/kg
Diphenylamine; N-phenylbenzeneamine					+	+		+	
Doxylamine succinate	-		epi studies		-	-	100 mg/kg	-	100 mg/kg
Ethanol (L)	+		epi studies		+	+	1-2 g/kg	+	17-30% caloric intake
Ethylene glycol					+	+	1400 mg/kg - many malformations	+	cleft palate, facial defects, open neural tube
N-Ethyl-N-nitrosourea; ENU				m +, f +	+	+	5-80 mg/kg	+	0.5 mM/kg
5-Fluorouracil	+	600 mg			+	+	12-37 mg/kg	+	10-40 mg/kg
Formamide					+	+	1 mL - resorptions, palate defects		
Furazolidone; N-(5-Nitro-2-furfurylidene)-3-amino-2-oxazolidone	-				-			-	750-1250 mg/kg
Glycerol; Glycerin; Trihydroxypropane					-	-	1 g/kg	-	1 g/kg
Glycerol formal					+	+	1 mL - septal defects	+	
Hydrazine					-	-	fetuses small and pale and edematous - 8 mg/kg		
4-Hydroxycoumarin	+				-			-	
7-Hydroxycoumarin					+	+		+	
m-Hydroxydilantin	+				+	+		+	
p-Hydroxydilantin	+		Case study		-	-	No defects (0.1 - 16 mg/kg given orally and subcutaneously)	-	No defects (100 - 300 mg/kg given intraperitoneally)

Substance	Rabbit	Malformations in Rabbits	Other Animals	Malformations in Other Animals	References
Dichloroacetate					Shepard 1992; Schardein 1993
Dichloroacetic acid					Schardein 1993; Shepard 1992
2,4-D; 2,4-dichlorophenoxyacetic acid					
Diethylene glycol	-	1000 mg/kg			Hellwig 1996
Dimethyl sulfoxide; DMSO			chicks	limb defects	Shepard 1992
Diphenhydramine hydrochloride; Benadryl (registered)	-	3-15 mg/kg			Smith 1983
Diphenylamine; N-phenylbenzeneamine					Sax 1998
Doxylamine succinate	-	100 mg/kg			Smith 1983
Ethanol (L)					Smith 1983
Ethylene glycol	-	via inhalation			Shepard 1992
N-Ethyl-N-nitrosourea; ENU	+	10 mg/kg	monkey	>40 mg/kg	Smith 1983
5-Fluorouracil					Smith 1983
Formamide					Shepard 1992
Furazolidone; N-(5-Nitro-2-furfurylidene)-3-amino-2-oxazolidone					Shepard 1992
Glycerol; Glycerin; Trihydroxypropane	-	1 g/kg			Food & Drug Research Lab 1974
Glycerol formal	+				Shepard 1992
Hydrazine			chicks	skeletal defects	Shepard 1992
4-Hydroxycoumarin	-				Smith 1983; Schardein 1993
7-Hydroxycoumarin	+				Schardein 1993
m-Hydroxydilantin	+				Schardein 1993
p-Hydroxydilantin	-	No defects (1.5 - 5.0 mg/kg given orally)			Schardein 1993

Substance	Human	Malformations in Humans	Human Reference Type	Reproductive Toxicity per NTP	Mammal	Rat	Malformations in Rats	Mouse	Malformations in Mice
Hydroxyurea			Case study		+	+	185-1000 mg/kg	+	exencephaly - 250 mg/kg
Isoniazid; Isonicotinic acid hydrazide	+	10 malformed children from 85 mothers exposed during the first four months of pregnancy (defects not stated); five children with severe encephalopathies after mothers treated with INH			-	-	16 mg/kg	-	100-300 mg/kg
Isonicotinic acid; Isonicotinic acid-2-isopropylhydrazide; 1-Methyl-formylhydrazine					+	+	100 mg/kg		
Maneb; [[1,2-ethanediy]bis[carbomodithioato]]-(2-)]manganese; manganous ethylenebis[dithiocarbamate]; Dithane; M-22; Manex; Trimanzol					+	+			
Methotrexate [(+) amethopterin]	+	oxycephaly, syndactyly			+	+		+	
Methylmercury chloride	+				+	+	35 mg/kg	+	30 mg/kg
Monosodium glutamate					-			-	No malformations or skeletal abnormalities (5.5 mg/kg i.p. to ICR mice on days 3,5,9, and 12 of gestation)
Nickel chloride; nickel dichloride					+	+	embryo lethality, some malformations		
Nicotine					+	+	hydrocephalus - 25 mg/kg	+	cleft palate, skeletal defects - 25 mg/kg
Nitrotriacetate					-	-	0.5% in diet	-	0.2% in diet
N-Nitrosodimethylamine; Dimethylnitrosamine					+			+	resorptions
Oxalic acid dihydrate				m - , f -	-	-	35 or 45 mg/kg		

Substance	Rabbit	Malformations in Rabbits	Other Animals	Malformations in Other Animals	References
Hydroxyurea	+	750 mg/kg	monkey	100 mg/kg	Schardein 1993; Copp 1990; Smith 1983
Isoniazid; Isonicotinic acid hydrazide	-	1.5-5 mg/kg			Smith 1983; Schardein 1993; Shepard 1992
Isonicotinic acid; Isonicotinic acid-2-isopropylhydrazide; 1-Methyl-formylhydrazine					Shepard 1992
Maneb; [[1,2-ethanediy]bis[carbomodithioato]]-(2-)]manganese; manganous ethylenebis[dithiocarbamate]; Dithane; M-22; Manex; Trimanzol					Schardein 1993
Methotrexate [(+) amethopterin]	+				Smith 1983; Schardein 1993
Methylmercury chloride					Smith 1983; Schardein 1993
Monosodium glutamate					Shepard 1992
Nickel chloride; nickel dichloride					Shepard 1992
Nicotine	-	stillbirths			Shepard 1992
Nitrotriacetate	-	250 mg/kg			Smith 1983
N-Nitrosodimethylamine; Dimethylnitrosamine					Shepard 1992
Oxalic acid dihydrate					Shepard 1992

Substance	Human	Malformations in Humans	Human Reference Type	Reproductive Toxicity per NTP	Mammal	Rat	Malformations in Rats	Mouse	Malformations in Mice
Pentachlorophenol; Penta; PCP					+	+	embryolethality - 15-30 mg/kg		
Permethrin; 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid (3-phenoxyphenyl)methyl ester				m -, f +	-	-	No defects (25 mg/kg given orally)	-	No defects (25 mg/kg given orally)
Phenytoin; Dilantin [registered]; 5,5-Diphenylhydantoin	-			m -, f +	+	+		+	cleft lip - 150 mg/kg
Phthalic acid				m -, f +	-	-			
Procarbazine	+	doubtful		m -, f +	+	+	150 mg/kg	+	20 mg/kg
Propylene glycol				m -, f +	-	-	0.2 mL		
Propylthiourea				m -, f +	+	+			
Pseudoephedrine [ephedrine-HCl]	+	1 case in 43 pregnancies							
Retinoic acid; all-trans-Retinoic acid; Tretinoin					+	+	20-80 mg/kg	+	50-200 mg/kg
13-cis-Retinoic acid					+	+	500 mg/kg	+	400 mg/kg
Saccharin	-				-	-	25 mg/kg	-	25 mg/kg
Salicylaldehyde					+	+		+	
Salicylic Acid					+	+		+	
Serotonin	+				+	+	1.5 mg/kg - anophthalmia, hydrocephalus, exencephaly, omphalocele	+	5-10 mg/kg hydrocephalus, exencephaly, hydronephrosis, renalagenesis, gastroschisis
Sodium acetate					-	-		-	1000 mg/kg
Sodium arsenate [dibasic heptahydrate]					+	+	30 mg/kg	+	45 mg/kg
Sodium arsenite; Sodium meta-arsenite									
Sodium cyclamate					-	-	100-500 mg/kg	-	5% in diet
Sodium salicylate; 2-Hydroxybenzoic acid monosodium salt				m -, f +	+	+		+	
Sodium selenate				m -, f +	-	-			

Substance	Rabbit	Malformations in Rabbits	Other Animals	Malformations in Other Animals	References
Pentachlorophenol; Penta; PCP					Shepard 1992
Permethrin; 3-(2,2- dichloroethenyl)-2,2- dimethylcyclopropanecarbo xylic acid (3- phenoxyphenyl)methyl ester	-				Goldey et al. 1994
Phenytoin; Dilantin [registered]; 5,5- Dihydrodihydroantoin	+	terminal digits	monkey		Schardein 1993; Shepard 1992
Phthalic acid	-	150 mg/kg	chicks	4% incidence of defects in head, eyes, and phocomelia or amelia - 3-20 mg	Shepard 1992
Procarbazine	+	100-300 mg/kg			Smith 1983
Propylene glycol					Shepard 1992
Propylthiourea					Schardein 1993
Pseudoephedrine [ephedrine-HCl]					Shepard 1992
Retinoic acid; all-trans- Retinoic acid; Tretinoin			monkey	10-40 mg/kg	Copp 1990; Smith 1983
13-cis-Retinoic acid					Smith 1983
Saccharin	-	5-25 mg/kg			Smith 1983
Salicylaldehyde					Sax 1998
Salicylic Acid					Schardein 1993
Serotonin					Shepard 1992
Sodium acetate					Kavlock 1987
Sodium arsenate [dibasic heptahydrate]					Smith 1983; Schardein 1993
Sodium arsenite; Sodium meta-arsenite			hamsters	increased incidence of malformations - 20 mg/kg	
Sodium cyclamate	-	50-250 mg/kg	-	500-2000 mg/kg - monkey	Shepard 1992; Smith 1983
Sodium salicylate; 2- Hydroxybenzoic acid monosodium salt	-				Schardein 1993
Sodium selenate	-		-	monkey	Fan 1992

Substance	Human	Malformations in Humans	Human Reference Type	Reproductive Toxicity per NTP	Mammal	Rat	Malformations in Rats	Mouse	Malformations in Mice
Solamargine				m -, f +	-	-			
.alpha.-Solanine				m -, f +	-	-			
.beta.2-Solanine				m -, f +					
Theophylline	-	76 women			+	-	359 mg/kg	+	396 mg/kg - resorptions
Tribromoacetic acid					+	-	in vitro -neural tube, eye, cardiovascular 3000 uM	+	600 mg/kg - cleft palate
Trichloroacetic acid	-	405 women			+	+	cardiovascular effects - 300 mg/kg		
Trichloroethylene					-	-	300-1800 ppm	-	300 ppm
Triethylene glycol					-	-		-	
Triethylene glycol dimethyl ether					+			+	craniofacial and skeletal - 1000 mg/kg
Urethane; Urethan; Ethyl carbamate					+	+		+	
Zinc chloride					+			+	

Substance	Rabbit	Malformations in Rabbits	Other Animals	Malformations in Other Animals	References
Solamargine					
.alpha.-Solanine			hamsters	7 malformations in 573 fetuses	Renwick 1984
.beta.2-Solanine					
Theophylline					Schardein 1993, Shepard 1992
Tribromoacetic acid					Hunter 1996
Trichloroacetic acid					Hunter 1996; Shepard 1992
Trichloroethylene					Smith 1983
Triethylene glycol	+				Stenger 1971; Bossert 1992; Neepers-Bradley 1994
Triethylene glycol dimethyl ether	+				Shepard 1992
Urethane; Urethan; Ethyl carbamate					Smith 1983; Schardein 1993
Zinc chloride					Shepard 1992